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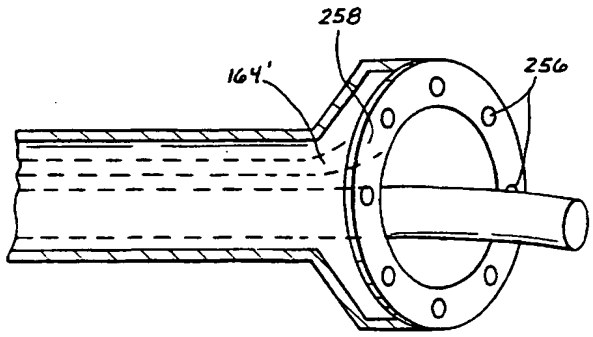

(57) Abstract: A system for delivering medicaments to tissue includes a tissue-removal and medicament-delivery device. The device includes a delivery member and an optical fiber formed together into a unitary structure by cladding. The optical fiber has an inlet for receiving laser energy from a laser energy source and an outlet for emitting laser energy. The delivery member has an inlet for receiving medicament from a medicament source and an outlet for injecting medicament. A handpiece is adapted to receive the ablating and injecting device in a controlled and movable relationship. In use, a distal end of the handpiece is placed against tissue to be ablated. The ablating and injecting device is advanced beyond the distal end of the handpiece and into the tissue while emitting laser energy from the optical fiber. The emitted laser energy ablates the tissue as the optical fiber advances. The ablating and injecting device is then retracted from the tissue, thereby resulting in a channel formed in the tissue. While the device retracts, medicament is injected from the delivery member into the channel, thereby providing a plug within the channel. Alternatively, medicament may be injected into the tissue surrounding the channel by delivering the medicament into the tissue surrounding the channel opening or delivering it directly into the channel wall. The medicament may include growth factor combined with a cellular matrix which enhances angiogenesis in the tissue or may include a gene that encodes for said growth factor, or any other therapeutic agent or gene therapy agent that promotes angiogenesis or any therapeutic agent for the treatment of cardiovascular disease. The medicament delivery system is particularly useful in cardiac applications for performing transmyocardial revascularization (TMR) in ischemic myocardium and promoting endothelial cell growth within the myocardium.

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METHODS AND APPARATUS FOR DELIVERING MEDICAMENT TO TISSUE

FIELD OF THE INVENTION

The present invention is directed to surgical methods and apparatus for delivering medicament to tissue. More particularly, the present invention is directed to surgical methods and apparatus for delivering medicament to tissue by first removing tissue to form a hole or channel in the tissue and then delivering medicament into the hole or channel or into the tissue surrounding the hole or channel. The methods and apparatus of the present invention may be applied in delivering growth factor to cardiac tissue during transmyocardial revascularization.

BACKGROUND OF THE INVENTION

Cardiomyopathy (*cardio* meaning "heart" and *myopathy* meaning "muscle disease") refers to a group of disorders that directly damage the muscle of the heart walls, or *myocardium*. In these disorders, all chambers of the heart are affected. The heart's function as a pump is disrupted, leading to an inadequate blood flow to organs and tissues of the body. Depending on the nature of the injury or abnormality in the heart muscle and the resulting structural changes in the heart chambers, one of three types of nonischemic (that is, not caused by heart attack) heart muscle disease may be present in a patient: *dilated congestive*, *hypertrophic*, or *restrictive*.

Dilated congestive cardiomyopathy damages the fibers of the heart muscle, weakening the walls of the heart's chambers. The chambers thereby lose some of their capacity to contract forcefully and pump blood through the circulatory system. To compensate for the muscle injury, the heart chambers enlarge or dilate which causes heart failure. Hypertrophic cardiomyopathy is characterized by a disorderly growth of heart muscle fibers causing the heart chambers to become thick walled and bulky. The thickening is generally most striking in the walls of the left ventricle, the chamber of the heart which pumps blood through the aorta to the vital organs and tissues of the body. The distorted left ventricle contracts, but the supply of blood to the brain and other vital organs may be inadequate because blood is trapped within the heart during contractions. Restrictive cardiomyopathy causes abnormal cells, proteins, or scar tissue to infiltrate the muscle and structures of the heart, causing the chambers to become stiff

and bulky. The heart may initially contract normally, but the rigid chambers restrict the return of blood to the heart.

Massive or multiple heart attacks may also lead to severe heart damage as a result of a disruption of blood supply to heart muscle. The damage can result in functional impairment and structural abnormalities similar to those found in the other types of cardiomyopathy. This type of heart disease, resulting from coronary artery disease, is called *ischemic cardiomyopathy* (*ischemic* meaning "lacking oxygen").

Severe heart injury caused by a major heart attacks or multiple smaller heart attacks may result in heart enlargement and thinning of the chamber walls, abnormalities which resemble those observed in dilated cardiomyopathy. Ischemic cardiomyopathy typically develops in patients with severe coronary artery disease, often complicated by other conditions such as diabetes and hypertension.

Although heart failure symptoms in ischemic cardiomyopathy are similar to those found in dilated cardiomyopathy, ischemic disease is more likely to be accompanied by symptoms of coronary artery disease, such as angina (which is chest pain resulting from reduced oxygen supply to the heart muscle). Diagnosis is typically based on a history of heart attacks and studies that demonstrate poor function in major portions of the left ventricle. The diagnosis can be confirmed by coronary angiography, which reveals areas of narrowing and blockage in the coronary blood vessels.

Patients with ischemic cardiomyopathy are treated with medications that relieve heart failure symptoms and improve blood flow through the diseased coronary arteries, such as nitroglycerin, some types of calcium channel blockers, and angiotensin-converting enzyme (ACE) inhibitors. When symptoms of heart failure and coronary artery disease cannot be controlled with medications, coronary angioplasty or surgery may be considered. Angioplasty and coronary artery bypass grafting may help increase blood flow to the heart, which in turn enhances heart muscle function.

When heart failure symptoms are advanced and cannot be improved by drug therapy or surgery, patients may be referred for a heart transplant. Patients with ischemic cardiomyopathy account for approximately one half of all heart transplant recipients. With a limited supply of donor hearts and complications resulting from heart transplant (such as organ rejection), surgeons have been exploring alternative procedures for treating severe ischemic

cardiomyopathy. One such procedure is *transmyocardial revascularization*, otherwise known more simply as "TMR."

TMR procedures revascularize, that is, form new channels, in the heart muscle or myocardium. The newly formed channels penetrate through the entire heart wall, which includes the *epicardium* (the outer layer of the heart), the *endocardium* (the inner lining of the heart), and the myocardium or muscular wall therebetween. As ischemic cardiomyopathy more often than not afflicts the left ventricle, the new channels are typically formed in the heart wall of this chamber of the heart. Accordingly, oxygenated blood from the lungs present in the left ventricle awaiting to be pumped through the aorta is able to flow directly into the newly formed channels to nourish the heart muscle.

Pioneering methods for performing TMR involved the use of needles for physically puncturing holes in the heart wall. These methods resulted in only a temporary delivery of blood to the myocardium because the holes quickly healed at the endocardium, preventing oxygenated blood from entering the myocardium. One of the more recent and exciting methods of performing TMR is through the use of lasers. It has been observed that new holes or channels formed in the heart wall by a laser tend to heal at the epicardium, which prevents blood loss, and promote blood perfusion into the ischemic region of the myocardium.

Lasers have proven to be a widely useful and applicable tool in modern medical techniques, particularly in minimally invasive surgical procedures. Technically speaking, a laser (the word *laser* being an acronym for *l*ight *a*mplification by *s*timulated *e*mission of *r*adiation) utilizes the natural oscillations of atoms or molecules between energy levels for generating coherent electromagnetic radiation. A laser is able to produce high-intensity and high-energy light at a single frequency. The energy of laser light is measured in joules (J), or watt-seconds (W-s), and the power of a laser is measured in watts (W).

One of the conventional surgical apparatus for performing TMR consists of a laser and an optical fiber. A surgeon places the end of the optical fiber against the epicardium to ensure that all the laser light is focused at the desired point, and then the laser is fired. In order to form the new channel completely through the heart wall and into the chamber, the surgeon needs to tactilely urge the optical fiber into and through the epicardium, the myocardium, and the endocardium. Because of the nature of ischemic cardiomyopathy, the thickness of the diseased myocardium is irregular and greater than normal. Accordingly, the surgeon needs to tactilely urge the optical fiber through the heart wall at each location. This procedure takes a certain

amount of time to accomplish safely and involves a certain amount of guesswork on the part of the surgeon. This procedure is complicated by the beating of the heart. Accordingly, the firing of the laser needs to be synchronized with the beating of the heart. In addition, irregularly shaped holes may result if the surgeon does not urge the optical fiber into the tissue at a constant rate. For example, a cavity within the new hole may be formed if the surgeon slowed down or paused briefly at a particular location because more tissue at that location would be ablated by the increase in laser energy emitted over time. In addition, the increase in emitted laser energy may cause excessive trauma to the surrounding tissue at that location.

In many surgical applications, it may be desired to drill as large a hole as possible. For example, in treating ischemic myocardium, holes with larger diameters have larger inner surface areas; accordingly, more blood is able to perfuse into the ischemic tissue. The difficulty in drilling relatively large holes (for example, about 1 mm) with laser ablation is that the area of the lasing plenum increases exponentially with an increase in the diameter of the hole (the *lasing plenum* being defined as the "bottom" of the hole subject to emitted laser energy). For example, the ratio between the areas of the lasing plenum of a hole with a 0.5-mm diameter and a hole with a 1-mm diameter is four. Conventional practice has been to increase the diameter of the optical fiber and, accordingly, the diameter of the laser beam to form larger holes. The power of the laser may also be increased. However, increasing the diameter of the laser beam results in an increase in the amount of energy emitted and, accordingly, an increase in the trauma of the surrounding tissue. In addition, the power of the laser energy can only be increased to a certain point until the capacity of the optical fiber is exceeded.

Accordingly, in view of the foregoing, it is an object of the present invention to provide methods and associated apparatus for delivering medicaments to tissue in a consistent and controlled manner.

It is another object of the present invention to provide surgical apparatus for forming either complete or partial holes in tissue and then delivering medicaments to the holes and/or to surrounding myocardium tissue.

It is a further object of the invention to provide surgical apparatus and methods for promoting angiogenesis and endothelial growth in the myocardium.

It is yet another object of the present invention to provide methods and associated apparatus for delivering medicaments to the myocardium while performing transmyocardial revascularization.

SUMMARY OF THE INVENTION

These and other objects are achieved by the surgical apparatus and associated methods of the present invention which provides a medicament delivery system which forms holes or channels in tissue by removing tissue and then delivers medicament to the hole or channel or to the tissue surrounding the hole or channel. Tissue is preferably removed with laser ablation but may be removed by other methods, for example, with high-frequency electrical energy.

The system for delivering medicament to tissue in accordance with the present invention may be utilized to form a hole or channel in tissue, for example, cardiac tissue (myocardium), and then to deliver medicament, for example, a therapeutic agent for the treatment of cardiovascular disease, a growth factor that promotes angiogenesis, a gene that encodes for said growth factor, or any other therapeutic agent or gene therapy agent that promotes angiogenesis, to the tissue by partially or fully filling the hole or channel with the medicament, or by injecting the tissue surrounding the hole or channel with the medicament. This process may be repeated a plurality of time to form and fill a plurality of holes and channels in a targeted area of tissue. In contrast to conventional systemic delivery approaches, the medicament-delivery system of the present invention delivers medicament in a controlled manner to specific targeted tissue.

The medicament-delivery system of the invention may form channels in targeted tissue by removing tissue with laser ablation. It has been found that tissue ablation with laser energy stimulates a natural biological process of angiogenesis in the heart. In addition, administering medicaments such as growth factors that promote angiogenesis have been found to promote angiogenesis in the heart. Accordingly, a synergistic stimulation and promotion of angiogenesis in the heart is created by augmenting the heart's natural angiogenic response to laser ablation with the delivery of growth factor to those areas of the myocardium which have been ablated. The coupling of the heart's natural response to the formation of channels with the delivery of growth factor into or adjacent to those channels provides a benefit to patients not heretofore possible.

In a broad aspect of the present invention, a system for delivering medicaments to tissue includes an ablating and injecting device and a handpiece. The ablating and injecting device includes an optical fiber and a delivery member formed together into a unitary structure with cladding. The optical fiber has an inlet for receiving laser energy from a laser energy source and an outlet for emitting laser energy. The delivery member has a lumen with an inlet for receiving medicament from a medicament source and an outlet for injecting medicament. The handpiece is adapted to receive the ablating and injecting device in a controlled and movable relationship.

In use, a distal end of the handpiece is placed against the target tissue. The ablating and injecting device is advanced beyond the distal end of the handpiece and into the tissue while emitting laser energy from the optical fiber. The emitted laser energy ablates the tissue as the optical fiber advances. The ablating and injecting device is then retracted from the tissue, thereby resulting in a channel formed in the tissue. While the device retracts, medicament is injected from the delivery member into the channel, thereby providing a plug within the channel. The medicament may include growth factor alone or in combination with a cellular matrix which enhances angiogenesis in the tissue.

Other aspects, features, and advantages of the present invention will become apparent to those persons having ordinary skill in the art to which the present invention pertains from the following description taken in conjunction with the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of an exemplary embodiment of a tissue drill of the present invention;

FIG. 1A is a cross-sectional view of an exemplary optical fiber of the invention taken along line 1A of FIG. 1;

FIG. 2A is a diagrammatic view of the exemplary tissue drill of the present invention, illustrating a handpiece receiving an optical fiber in a retracted position;

FIG. 2B is a diagrammatic view similar to that of FIG. 2A, illustrating the optical fiber in an advanced position;

FIG. 3A is a diagrammatic view of an exemplary handpiece of the tissue drill of the present invention, illustrating the handpiece disassembled;

FIG. 3B is a diagrammatic view similar to that of FIG. 3A, illustrating the handpiece assembled;

FIG. 4 is a schematic view of an exemplary optical fiber of the present invention, particularly illustrating an eccentric configuration of an outlet portion of the optical fiber;

FIG. 5 is a schematic view of an end surface of the optical fiber illustrated in FIG. 4;

FIG. 6 is a schematic view of another exemplary optical fiber of the present invention;

FIG. 7 is a schematic view of an end surface of the optical fiber illustrated in FIG. 6;

FIG. 8 is a diagrammatic view of an exemplary end surface of an optical fiber of the present invention, particularly illustrating a relationship between emitted laser energy and position of the end surface;

FIG. 9 is a schematic view of an exemplary source of laser energy of the present invention;

FIG. 10A is a schematic view of an exemplary tissue drill of the present invention, particularly illustrating a step of a preferred tissue-drilling procedure implementing the tissue drill;

FIG. 10B is a view similar to that of FIG. 10A, illustrating a subsequent step in the tissue-drilling procedure;

FIG. 10C is a view similar to that of FIG. 10B, illustrating another subsequent step in the tissue-drilling procedure;

FIG. 10D is a view similar to that of FIG. 10C, illustrating yet another subsequent step in the tissue-drilling procedure;

FIG. 11 is a schematic view of tissue in which a hole has been drilled according to an exemplary method of the invention;

FIG. 12 is a schematic view of tissue in which a hole has been drilled according to another exemplary method of the invention;

FIG. 13 is a perspective view of an exemplary medicament delivery system configured in accordance with the present invention;

FIG. 14 is a schematic cross-sectional view of an exemplary ablating and injecting device for use in the medicament delivery system of the present invention;

FIG. 15 is a schematic view of an end surface of the ablating and injecting illustrated in FIG. 14;

FIG. 16 is a schematic view of an exemplary source of laser energy and medicament for use in the medicament delivery system of the present invention;

FIG. 17A is a schematic view of an exemplary medicament delivery system of the present invention, particularly illustrating a step of a preferred medicament-delivery procedure of the invention;

FIG. 17B is a view similar to that of FIG. 17A, illustrating a subsequent step in the medicament-delivery procedure;

FIG. 18 is a perspective view of a tissue-removal and medicament-delivery system in accordance with the invention, particularly illustrating a coupling assembly of the invention;

FIG. 19 is a cross-sectional view of an exemplary coupling assembly taken along line 19—19 of FIG. 18, with medicament injection and supply units shown schematically;

FIG. 20 is a diagrammatic view of an alternative embodiment of an exemplary ablating and injecting device for use in the medicament delivery system of the present invention;

FIG. 21 is a diagrammatic view of another embodiment of an exemplary ablating and injecting device for use in the medicament delivery system of the present invention;

FIG. 22 is a cross-sectional view of a tissue-removal and medicament-delivery device of the present invention, particularly configured to remove tissue with high-frequency electrical energy;

FIG. 23 is a cross-sectional view of an alternative embodiment of a tissue-removal and medicament-delivery device of the present invention;

FIG. 24 is a schematic view of a step of a tissue-removing procedure incorporating the device of FIG. 22 or 23, particularly removing tissue with high-frequency electrical energy according to the invention;

FIG. 25 is a schematic view of a medicament-delivery step of the invention, particularly illustrating the delivery of medicament to tissue surrounding a hole or channel formed in tissue;

FIG. 26 is a cross-sectional view of another embodiment of an electrical-energy tissue-removal and medicament-delivery device in accordance with the invention;

FIG. 27 is a schematic view of another embodiment of a medicament-delivery system of the invention, particularly illustrating an ablating and injecting device received within a catheter with rifling;

FIG. 28 is a cross-sectional view of the medicament-delivery system of FIG. 27;

FIG. 29 is a developmental view of an exemplary catheter with rifling for use in the medicament-delivery system of FIG. 27;

FIG. 30 is a schematic view of an exemplary medicament delivery system of the present invention, illustrating needles around the perimeter of the head portion of the handpiece;

FIG. 31 is a schematic view of the end surface of the head portion of FIG. 30;

FIG. 32 is a schematic view of the embodiment of FIG. 30, particularly illustrating a step of a preferred medicament-delivery procedure of the invention;

FIG. 33 is a schematic view of another exemplary embodiment of the head portion of the handpiece, illustrating nozzles around the perimeter of the head portion of the handpiece;

FIG. 34 is an end view of yet another exemplary embodiment of the head portion of the handpiece, illustrating ports around the perimeter of the head portion of the handpiece;

FIG. 35 is a perspective view of an alternative embodiment of a tissue-removal and medicament-delivery device of the present invention utilizing a single delivery lumen;

FIG. 36 is a schematic cross-sectional view of the embodiment of FIG. 35;

FIG. 37 is a perspective view of yet another embodiment of a tissue-removal and medicament-delivery device of the present invention utilizing a single delivery lumen;

FIG. 38 is a schematic cross-sectional view of yet another embodiment of of the device of the present invention utilizing at least one vacuum lumen and at least one delivery lumen;

FIG. 39 a schematic cross-sectional view of a step of an alternate exemplary embodiment of an electrical-energy tissue-removal and medicament-delivery device of the present invention; and

FIG. 40 is a schematic cross-sectional view of the embodiment of FIG. 39, particularly illustrating a step of a preferred medicament-delivery procedure of the invention.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

Referring to the drawings in more detail, in FIG. 1 an exemplary embodiment of a tissue drill 50 of the present invention is illustrated in conjunction with a source of laser energy 52. Exemplary tissue drill 50 forms holes or channels in tissue by laser ablation in a consistent, controllable, and programmable manner. The first portion of the following description focuses on the principles of tissue ablation and the forming of channels in tissue. These principles of the present invention are then readily applied to a system for delivering medicaments to the tissue in which the channels are formed, which will be discussed in more detail below.

Ablation is the process of fragmenting long molecules into short gaseous molecules. Much of the tissue in living organisms, including the human body, is made up mostly of water (e.g., about 75%) with organic material making up the remaining portion. The molecules of organic material consist of atoms of carbon, nitrogen, oxygen, and hydrogen that are attached together through covalent bonds. Ablation is the process of breaking these covalent bonds. Tissue drill 50 utilizes the ablation process to break molecules of tissue apart, thereby forming holes or channels in the tissue. The ablation process will be discuss in more detail below.

Exemplary tissue drill 50 includes a handpiece 54 for manipulation by a user and an optical fiber 56, which is shown in FIG. 1A, for transmitting laser energy from laser energy source 52. Optical fiber 56 has an outlet portion 58 for emitting laser energy. Outlet portion 58 functions substantially as a drill bit. In operation, outlet portion 58 is moved from a retracted position (which is shown in the solid line) to an advanced position (which is shown by the phantom line) while emitting laser energy. Arrow A represents outlet portion 58 moving to the advanced portion, and arrow L represents laser energy emitted from outlet portion 58. Tissue is ablated by laser energy as outlet portion 58 is advanced, thereby forming a hole or a channel in the tissue. Exemplary tissue drill 50 may also rotate outlet portion 58 while moving to the advanced position, which is represented by arrow R. After reaching the advanced position, outlet portion 58 may be withdrawn to the retracted position, which is represented by arrow B. The advancing and retracting of outlet portion 58 is preferably along a central axis of optical fiber 56. Any rotation of outlet portion 58 is preferably about the central axis of optical fiber 56. The axial and rotational movement of outlet portion 58 will be discussed in more detail below.

Exemplary outlet portion 58 of optical fiber 56 has an end surface 60 with an outlet 62 from which laser energy is emitted. Outlet 62 is preferably offset from or eccentric to the central axis of outlet portion 58 so that as outlet portion 58 rotates, outlet 62 rotates about the central axis. Accordingly, laser energy emitted from outlet 62 as outlet portion 58 rotates is not focused at a single point but is rather distributed about the central axis. Alternatively speaking, the eccentric relationship of outlet 62 with respect to the central axis of outlet portion 58 preferably produces a gradient of laser energy as outlet portion 58 axially advances, with the highest level of laser energy at the central axis, which energy decreases toward a peripheral edge. The eccentricity of outlet portion 58 will also be discussed in more detail below.

Handpiece 54 may be implemented according to a variety of configurations. For example, handpiece 54 may be a flexible catheter utilized in endovascular procedures and having a plurality of lumens to facilitate visualization, flushing, and aspiration. In this regard, outlet portion 58 may advance beyond a distal end of the catheter to vascularize tissue, such as on the inside the left ventricle of the heart. Alternatively, handpiece 54 may be formed as a trocar sheath and positioned intercostally (i.e., between the ribs) for tissue access. Handpiece 54 may also be formed in a gooseneck-like configuration with a plurality of articulated joints which may be bent to assume and retain a particular shape. Moreover, handpiece 54 may be a conduit with

flexible cable sheathing. Accordingly, in a general sense, handpiece 54 provides a "user interface" for delivering outlet portion 58 to a target site, which may be accomplished either by direct physical manipulation by a surgeon or by programmed mechanical control.

An exemplary handpiece of the present invention is illustrated in FIGS. 2A and 2B. Exemplary handpiece 54 may include a body portion 64 and a coupling portion 66. Exemplary body portion 64 has a distal end 68. Exemplary coupling portion 66 is adapted or configured to receive optical fiber 56 in a controlled and axially movable relationship so that outlet portion 58 may be advanced beyond distal end 68 of body portion 64. In addition, coupling portion 66 may be adapted to receive optical fiber 56 in a rotatable relationship so that at least outlet portion 58 of optical fiber 56 may rotate. If handpiece 54 is configured as a catheter or similar flexible tubular member, the inner surface of the tubular member serves as a coupling portion by receiving optical fiber 56 in a controlled, axially movable, and/or rotatable relationship.

The retracted position of outlet portion 58 as shown in FIG. 2A may be defined as a position in which end surface 60 is positioned substantially at or near distal end 68 of body portion 64. Accordingly, end surface 60 may project slightly beyond distal end 68 or, alternatively, may be either proximal to or substantially aligned (or coplanar) with distal end 68. The advanced position of outlet portion 58 as shown in FIG. 2B may be defined as a position in which end surface 60 with outlet 62 projects a distance *d* beyond distal end 68 of body portion 64. As will be discussed in more detail below, distance *d* at which end surface 60 projects beyond distal end 68 is preferably predetermined, adjustable, and/or programmable.

With additional reference to FIGS. 3A and 3B, exemplary coupling portion 66 may include a drive which is comprised of a tubular member 70 and a collar 72. Tubular member 72 receives optical fiber 56 and may have a chuck 74 for retaining optical fiber 56 thereto. Tubular member 72 may also have annular threading 76 formed along a length thereof. Collar 72 is disposed within body portion 64 and has complementary inner threading 78. Exemplary tubular member 72 is slidably and rotatably receivable within body portion 64 with annular threading 76 engaging with inner threading 78 of collar 72, as shown in FIG. 3B. Accordingly, rotation of tubular member 70 causes tubular member 70 to move axially. As optical fiber 56 is retained by chuck 74, optical fiber 56 with outlet portion 58 moves axially with tubular member 70. In an alternative embodiment of handpiece 54 such as a catheter, rather than disposing coupling portion 66 and a drive on handpiece 54, these elements may be provided at a proximal location, such as at laser apparatus 52. In this regard, catheter-configured handpiece 54 retains optical

fiber 56 within a body portion which prevents buckling and which delivers outlet portion 58 to a target site but which is substantially free of coupling and drive apparatus.

Referencing FIG. 4, in addition to outlet portion 58, exemplary optical fiber 56 has an elongate portion 80. A core 82 and a cladding 84 define optical fiber 56 and extend along elongate portion 80 and outlet portion 58. Core 82 has an inlet 86 for receiving laser energy and outlet 62 (see also FIG. 1) for emitting laser energy. Core 82 and cladding 84 may be made of high-purity silica glass or sapphire, with core 82 having a higher index of refraction than that of cladding 84 so that modulated pulses of laser energy move along core 82 without penetrating cladding 84. Although optical fiber 56 may be configured according to any dimensions, for many applications a length l_e of elongate portion 80 may range from about 0.5 meter (m) to more than 2 m to provide a surgeon with sufficient maneuverability, and a length l_o of outlet portion 58 may range up to about 50 millimeters (mm) so that holes of different lengths may be formed in tissue. For applications other than medical, optical fiber 56 may be dimensioned accordingly to accomplish the particular application.

Core 82 of optical fiber 56 has an axis E along elongate portion 80 and an axis O at outlet 62. With additional reference to FIG. 5, core 82 along outlet portion 58 angles away from and is oblique to core 82 along elongate portion 80. At end surface 60, axis O of core 82 at outlet 62 is offset from or eccentric to axis E of core 82 of elongate portion 80 by a distance δ. Accordingly, laser energy emitted from outlet 62 is distributed about axis E as optical fiber 56 rotates about axis of rotation E. Further, the distribution of laser energy is across the entire surface area of end surface 60 as optical fiber 56 make one complete revolution. At end surface 60, outlet 62 may be configured so that axis O of core 82 is either oblique to axis E or, as shown, parallel to axis E.

An alternative exemplary embodiment of optical fiber 56 is illustrated in FIGS. 6 and 7. In addition to core 82 and cladding 84, exemplary optical fiber 56 may include auxiliary cladding 88 disposed about outlet portion 58. Similar to the embodiment shown in FIG. 4, to offset axis O of outlet 62 from axis of rotation E by distance δ, core 82 of outlet portion 58 is oblique to core 82 of elongate portion 80. Auxiliary cladding 88 compensates for the oblique relationship of core 82 (and cladding 84) of outlet portion 58 with respect to core 82 (and cladding 84) of elongate portion 80. Auxiliary cladding 88 accordingly provides a preferred cylindrical configuration of outlet portion 58 so that outlet portion 58 rotates about axis E as elongate portion 80 rotates about axis E. Further, in addition to axis O at outlet 62 being eccentric to

axis E, axis O of core 82 may be oblique to axis E at outlet 62, rather than a parallel relationship as shown in FIG. 4.

As illustrated in FIGS. 6 and 7, end surface 60 (including outlet 62) is substantially perpendicular to axis E of exemplary optical fiber 56. To form the perpendicular relationship, core 82 and cladding 84 are ground or polished at an angle oblique to axis O, thereby removing portions of core 82 and cladding 84 shown by phantom line P. Accordingly, exemplary end surface 60 is substantially planar. Alternatively, end surface 60 may be convex, concave, or other configuration depending upon a particular implementation of outlet portion 58.

With particular reference to FIG. 7, end surface 60 of exemplary optical fiber 56 has a circumference C_{es} defined along an outer edge 90, and outlet 62 of core 82 has a circumference C_o defined along outer edge 92. Circumference C_{es} and circumference C_o are coextensive along an arc length α of outer edges 90 and 92. This relationship allows laser energy to be emitted from outlet 62 at outer edge 90 of end surface 60. As outlet portion 58 rotates, laser energy is emitted along circumference C_{es} of rotating end surface 60. Arc length α may range from a single tangent point to several seconds, minutes, or degrees as desired.

Diameter d_o of outlet 62 is preferably greater than about one half of diameter d_{es} of end surface 60. Accordingly, outlet 62 has a surface area which is at least one quarter of that of end surface 60. This relationship in surface area allows laser energy to be emitted from a substantial percentage of end surface 60. Further, laser energy is not emitted from the entire end surface 60 simultaneously but rather over the time it takes outlet portion 58 to make one revolution about axis E. An exemplary commercial embodiment of optical fiber 56 for use in transmyocardial revascularization entails a diameter d_{es} of end surface 60 (and outlet portion 58 of approximately 1 mm and a diameter d_o of outlet 62 of approximately 0.6 mm. Generally speaking, the dimensions of outlet portion 58 are determined by the type of procedure being performed and the desired size of the hole, with diameter d_o of outlet 62 being at least one half of diameter d_{es} of end surface 60. For example, if a hole with a 1.5-mm diameter is desired, then diameter d_{es} of end surface 60 (and outlet portion 58) should be about 1.5 mm; diameter d_o of outlet 62 may accordingly range from about 0.75 mm to slightly less than 1.5 mm, but is preferably about 0.8 mm. For many medical applications, it is contemplated that diameter d_{es} of end surface 60 may range from about 0.2 mm to more than 2.5 mm, with diameter d_o of outlet 62 ranging from less than about 0.1 mm to about 2 mm or more. For specific medical applications such as transmyocardial revascularization (which will be discussed below), diameter d_{es} of end surface

60 may range from about 0.6 mm to about 2 mm, with diameter d_o of outlet 62 ranging from about 0.3 mm to about 1 mm.

With additional reference to FIG. 8, end surface 60 is schematically illustrated during rotation, with outlet 62 shown at progressive instances in time t_1, t_2, t_3, and t_4 while rotating about axis E. Because of the relationship between the surface areas of end surface 60 and outlet 62, laser energy is continuously emitted from an area 94 of end surface 60. In other words, area 94 represents an intersection of the positions of outlet 62 at every instance of time while rotating about axis E. Laser energy is accordingly emitted at intervals at other areas of end surface 60 depending upon the position of outlet 62 at a particular instance in time.

The relationship between laser energy emitted from exemplary end surface 60 per revolution of outlet 62 about axis E with respect to distance from axis E is illustrated graphically in FIG. 8. Emitted laser energy per revolution of outlet portion 58 decreases from a constant level at area 94 to a lower level at outer edge 90 of end surface 60. In the graph, outer edge 90 is a distance from axis E substantially equal to radius r_{es} of end surface 60. Depending upon a particular configuration of exemplary end surface 60 and outlet 62, the decrease in laser energy or flux with respect to position may be a linear function as shown or a nonlinear function. Also, the relative level of energy per revolution at area 94 and at radius r_{es} is illustrative only, as the level of energy at the periphery of end surface 60 may vary according to the particular surgical procedure. For example, the energy flux at radius r_{es} may be at a relatively low level when compared to the constant level at area 94.

In accordance with this energy distribution per revolution of the present invention, while ablating tissue to form a hole, the transference of laser energy to peripheral or surrounding tissue is less than at a center of the hole being formed. This distribution of laser energy may limit trauma to tissue in which holes or channels are formed. More specifically, as outlet portion 58 moves through tissue while rotating and emitting laser energy, outer edge 90 of end surface 60 is adjacent to and contacts the surrounding tissue which defines the hole being formed. As the level of emitted laser energy at outer edge 90 is lower than that centered about axis E (which essentially defines the center of the hole being formed), damage to the surrounding tissue is reduced, resulting in less trauma to the tissue. It is believed that tissue with a relatively low level of trauma has a likelihood to experience angiogenesis, or the formation of new blood vessels in the tissue. This reduced-trauma feature of the present invention will be discussed in more detail below.

An exemplary process to form an eccentric outlet portion 58 as described above involves placing the distal end of optical fiber 56 within a Teflon® tube at an angle, with cladding 84 contacting the inner surface of the tube at one point. The tube may then be filled with epoxy which surrounds the distal end of optical fiber 56 except at the point at which cladding 84 contacts the tube. After the epoxy has cured and hardened, the tube is removed, and the distal surface of the epoxy and optical fiber 56 is polished to define end surface 60 at the point where cladding 84 defines an annular edge of outlet portion 58. End surface 60 may also be formed with a lens to control the emission of the laser energy in a particular manner. An inner diameter of the tube for forming outlet portion 58 essentially determines the diameter of outlet portion 58 (i.e., diameter d_{es} of end surface 60). According to this process, optical fibers 56 having outlet portions 58 of different diameters may be formed, enabling surgeons to form holes with a variety of diameters. In addition, a plurality of outlet portions 58 each having a different diameter may be formed, each of which being able to be coupled to an optical fiber, so that a set of interchangeable "drill bits" is at a surgeons disposal during a particular procedure. Optical fiber 56 may be reusable or disposable, as may outlet portion 58 and handpiece 54.

With further reference to FIGS. 1 and 3A, exemplary of handpiece 54 may include a head portion 96 connectable to a distal end of body portion 64 by a neck 98. Distal end 68 of body portion 64 is accordingly defined by a tissue end 100 of head portion 96. Exemplary head portion 96 may be conical so that tissue end 100 has a larger diameter than body portion 64. Tissue end 100 provides a working surface or a tissue-engaging surface for positioning handpiece 54 over and against a surgical site in which a channel is to be drilled into tissue. Exemplary head portion 96 may also have an aperture 102 formed therein. Aperture 102 may function as a window for viewing a surgical site when tissue end 100 is placed against tissue. Aperture 102 may also function as a vent for exhausting gases which may be generated by laser energy ablating tissue. As shown in FIG. 1, exemplary neck 98 may be angular to enhance the positioning of head portion 96 against tissue. In this regard, neck 98 may be configured as a gooseneck with articulable joints for assuming and retaining a desired shape. Exemplary head portion 96 and neck 98 are preferably tubular, thereby providing an inner continuum with body portion 64 in which optical fiber 56 is receivable.

In particular procedures, it may be preferable to know where a hole has been drilled in tissue. However, the nature of the tissue or the size of the hole may render it difficult for the surgeon to determine where a hole has already been formed. Accordingly, the newly formed

hole drilled in tissue may be marked. In this regard, head portion 96 may include apparatus for marking where a hole has been drilled in tissue. For example, tissue end 100 may have an inking device which dispenses biocompatible ink or dye on the tissue where a hole has been formed. The ink may be applied to the tissue through direct contact with tissue end 100 or, for example, by spraying. Exemplary handpiece 54 may have a reservoir for storing and dispensing a colored liquid or a particulate solid to the tissue. Fluorescent material may be used to enhance visualization. Other indicia may be applied to the tissue by handpiece 54 or head portion 96 at the target site; for example, alphanumeric indicia may indicate the parameters of the laser energy emitted from outlet 62 to form a particular hole.

With further reference to FIGS. 2A to 3B, exemplary coupling portion 66 may include a spring 104 receivable against a seat 106 formed on a distal end of collar 72, and a stop 108 disposed on a distal portion of tubular member 70. Spring 104 and stop 108 define a mechanism for controlling a position of tubular member 70 within body portion 64, and may be configured to facilitate the advancement and retraction of tubular member 70.

Exemplary source of laser energy 52 is illustrated in FIG. 9. Laser energy source 52 includes a laser 110 for generating laser energy L. Exemplary laser energy source 52 may include a drive assembly 112 for operatively associating with handpiece 54 and optical fiber 56, and may also include a control unit 114 with a user interface 116. Exemplary drive assembly 112 may include a coupler 118 for connecting with optical fiber 56, optics 120 for modifying laser energy L as desired, and a drive/motor 122. Exemplary coupler 118 is associated with optics 120 for transferring laser energy L from laser 110 to the inlet of optical fiber 56. Exemplary coupler 118 is also associated with drive/motor 120 for rotating optical fiber 56.

As discussed above in reference to FIGS. 2A and 2B, exemplary coupling portion 66 of handpiece 54 translates rotational movement of optical fiber 56 to axial movement to advance and to retract outlet portion 58. Exemplary drive assembly 112 preferably rotates optical fiber 56. For example, coupler 118 may secure and retain a proximal end of optical fiber 56, with motor/drive 122 rotating coupler 118 which also rotates optical fiber 56. Drive assembly 112 may rotate optical fiber 56 in a first direction, for example, as shown by arrow R_1 in FIG. 2A, to cause optical fiber 56 to advance axially as shown by arrow A. When outlet portion 58 reaches the desired advanced position, drive assembly 112 may then rotate optical fiber 56 in an opposite second direction, as shown by arrow R_2 is FIG. 2B, to cause optical fiber 56 to retract axially as shown by arrow B. Exemplary drive assembly 112 may oscillate optical fiber 56 (that

is, rotate optical fiber 56 clockwise and counterclockwise as shown by arrows R_1 and R_2) so that outlet portion 58 reciprocates between the retracted position and the advance position.

Exemplary laser energy source 52 preferably controls when laser energy L is emitted from outlet portion 58 of optical fiber 56. For example, control unit 114 in association with laser 110 and drive assembly 112 may limit the emission of laser energy L to only when outlet portion 58 moves to the advance position. Laser energy L may then be terminated during the retraction of outlet portion 58. Alternatively, if drive assembly 112 is reciprocating outlet portion 58, laser energy L may be transmitted only during the advancing stroke of outlet portion 58; the emission of laser energy L may then be terminated at the end of the advancing stroke. The termination of laser energy L upon reaching the advanced position is preferably automatic and controlled by laser energy source 52. Alternatively, laser energy L may be terminated by a device such as a pressure sensor which determines when the distal end of outlet portion 58 advanced completely through a section of tissue, e.g., the wall of the heart. This control of laser energy L is preferable during particular applications of tissue drill 50, which will be discussed in more detail below.

With further reference to FIG. 1A, optical fiber 56 is preferably received within a housing 124. In addition to protecting optical fiber 56, exemplary housing 124 constrains any torsional flexing or bending of optical fiber 56 which may result from the rotation by drive assembly 112. Exemplary optical fiber 56 may include a complementary coupler 126 for connecting with coupler 118 of laser energy source 52. Complementary coupler 126 preferably provides a releasable association with coupler 118 so that other optical fibers in accordance with the present invention may be connected to laser energy source 52. Exemplary housing 124 preferably extends between coupler 126 and chuck 74 of coupling portion 66 to provide integral protection of optical fiber 56 between laser energy source 52 and handpiece 54.

Exemplary laser energy source 52 may control a number of parameters of tissue drill 50, including distance *d* at which outlet portion 56 advances, a speed at which outlet portion 56 advances, and a level at which laser energy is emitted from outlet 62. Control unit 114 in association with user interface 116 preferably controls, programs, monitors, and/or adjusts each of these parameters depending upon a particular tissue-drilling application. For example, one the many applications of tissue drill 50 is for drilling holes or channels into or through heart walls. This procedure is known as *transmyocardial revascularization* or, more simply, as

TMR. FIGS. 10A through 10D schematically illustrate an exemplary TMR procedure implementing tissue drill 50 of the present invention.

A heart wall 130 is illustrated in FIG. 10A and includes myocardium, or heart muscle, 132 positioned between an outer serous layer or epicardium 134 and an inner membrane or endocardium 136. It has been found to be medically beneficial to revascularize the myocardium of patients suffering from severe ischemic cardiomyopathy. The revascularization of the myocardium 132 involves forming new channels in the tissue. By implementing exemplary tissue drill 50 of the present invention, new channel may be formed in the myocardium in a controlled, consistent, and programmable manner.

Prior to a TMR procedure, the level at which laser 110 is to generate laser energy L and the frequency at which laser energy L is to be pulsed may be determined. In addition, distance *d* at which outlet portion 58 is to advance beyond distal end 68 and the speed at which outlet portion 58 is to rotate may be determined. These parameters may be stored in control unit 114 and varied or programmed via user interface 116.

During the TMR procedure, access to the patient's chest cavity is provided, preferably by a minimally invasive procedure such as an intercostal incision using trocar sheaths. Access to the patient's heart is then provided, for example, by incising the pericardium. With outlet portion 58 in the retracted position, a surgeon may then maneuver head portion 96 of handpiece 54 into the chest cavity and position tissue surface 100 against the epicardium 134, as shown in FIG. 10A. As discussed above, outlet portion 58 may project slightly beyond distal end 68 (that is, tissue end 100) when in the retracted position to provide the surgeon with a tactile feel of the position of end surface 60 on the epicardium 134.

When in the desired position on the epicardium 134, tissue drill 50 may be activated. This activation may be accomplished manually by an assistant via user interface 116 or by the surgeon with a foot or a hand trigger. Alternatively, activation of tissue drill 50 may be synchronized with the electrical activity of the heart through the use of an electrocardiogram (EKG) machine. Activation of tissue drill 50 causes laser energy source 52 to generate and transmit laser energy to optical fiber 56. Activation also causes optical fiber 56 to rotate and advance outlet portion 58 through the epicardium 134 and into the myocardium 132 of the heart wall 130, as shown in FIG. 10B.

Outlet portion 58 continues to advance through the myocardium 132 and through the endocardium 136. When end surface 60 of outlet portion 58 has advanced through the

endocardium 136 and is positioned within the left ventricle of the patient's heart as shown in FIG. 10C, the emission of laser energy is preferably terminated, and the outlet portion 58 is retracted. A new channel 138 through the heart wall 130 results from this procedure as shown in FIG. 10D. Oxygenated blood from the left ventricle may enter the new channel 138 through the endocardium 136 and perfuse the tissue of the myocardium 132 surrounding the new channel 138. When handpiece 54 is configured as a catheter, outlet portion 58 advances through the endocardium 136 and then into the myocardium 132. Because outlet portion 58 may be programmed to advance a predetermined distance, outlet portion 58 may either continue to advance completely through the epicardium 134 or begin to retract the predetermined distance within the myocardium 132, thereby forming a hole in the heart wall 130 rather than a channel through the heart wall 130.

As mentioned above, reduced trauma to the myocardium 134 surrounding the new channel 138 results from the eccentric relationship between outlet 62 and rotational axis E. This reduced trauma may enable the surrounding tissue to regenerate vascular tissue from the new channel 138 and into the myocardium 134 or to experience angiogenesis. In addition to the eccentricity of outlet portion 58, the level of trauma inflicted on the surrounding tissue is mediated by the level of laser energy emitted from outlet 62, which will now be discussed.

With reference to FIG. 9, the energy level at which laser energy L is generated and transmitted to optical fiber 56 may be varied, programmed, and controlled according to each tissue-drilling application. For example, tissue drill 50 may be configured for drilling holes in all types of animal tissue and plant tissue, as well as other substances. The parameters which define the characteristics of laser ablation include frequency, energy per channel, pulse width, and pulse rate. As mentioned earlier, ablation is a process of breaking bonds between atoms in molecules by adding energy to the molecules. One preferred level of the laser energy L for TMR applications is to limit the energy per pulse to less than about 100 milliJoules per square millimeter of area (mJ/mm^2). More preferably, an energy per pulse of about 30 mJ/mm^2 has been found to ablate cardiac tissue at a substantially reduced level of trauma. The energy per pulse of laser 110 may be varied according to specific tissue-drilling procedures.

With further reference to FIGS. 3A and 3B, the drive may be configured to control the rate at which outlet portion 58 advances and retracts. The rate of advancement is controlled by the speed at which optical fiber 56 rotates and the pitch of the complementary threading of collar 72 and tubular member 78. For smooth and continuous operation, it has been determined that optical fiber

56 and, accordingly, outlet portion 58 should rotate at a speed under about 5,000 revolutions per minute (RPM). For TMR applications of tissue drill 50, a rotational speed ranging from about 1,000 RPM to about 2,000 RPM is preferred. In this regard, a specific TMR configuration of tissue drill 50 may be as follows. Optical fiber 56 may rotate at about 1,340 RPM. The pitch of threading 76 and 78 may be configured so that outlet portion 58 advances at a rate of about 15.5 millimeters per second (mm/s). With a rotational speed of 1,340 RPM, it takes about 46 milliseconds (ms) for outlet portion 58 to complete one rotation. For TMR applications, laser 110 may emit pulses of laser energy L of about 20 nanoseconds (ns) in duration, with each pulse being separated by about 4 ms. The pulse rate may be about 10 pulses per revolution (or at about every 36° of rotation) or about 240 pulses per second.

Rather than advancing and retracting outlet portion 58 at a constant rate as described above, tissue drill 50 may be configured such that outlet portion 58 moves at varying rates of speed between the retracted and advanced positions. The slower outlet portion 58 advances (or retracts) while emitting laser energy L, the more tissue that becomes ablated because the tissue is subject to more laser energy over time. Accordingly, a hole may be formed with a diameter greater than diameter d_{es} of end surface 60 (and outlet portion 58) by advancing outlet portion 58 at a speed which allows laser energy L to ablate a greater amount of tissue. Alternatively, the power of laser energy L may also be varied during the advancement of outlet portion 58 so that the tissue is subjected to more or less laser energy L. Generally speaking, a surgeon may program tissue drill 50 to ablate tissue at varying levels of energy per unit time to form holes of varying desired diameters or configurations. The energy per unit time may be adjusted by varying either the speed at which outlet portion 58 advances (which varies the time the tissue is subject to laser energy) or the level of laser energy, or both.

In order to form the substantially cylindrical hole 138 shown in FIG. 10D, tissue drill 50 advanced outlet portion 58 at a substantially constant speed, and laser energy source 52 emitted laser energy at a substantially constant level. However, if a conical-shaped hole 140 as shown in FIG. 11 is desired, with the apex of the hole 140 positioned at the epicardium 134 and the base of the hole 140 positioned at the endocardium 136, then tissue drill 50 may be configured to advance outlet portion 58 at a decreasing rate (i.e., moving at a slower and slower speed) while advancing through the heart wall 130 from the epicardium 134 to the endocardium 136. Accordingly, a greater amount of tissue is ablated as outlet portion 58 advances at a slower speed. The resulting hole 140 has a diameter substantially equal to diameter d_{es} of outlet portion 58 at the epicardium 134 and a diameter

larger than diameter d_{es} at the endocardium 136. By forming the hole 140 with a relatively large diameter at the endocardium 136 improves the patency of the hole and, therefore, the perfusion of the blood into the myocardium 132. In addition, by forming a hole with as small a diameter as possible at the epicardium 134 minimizes bleeding and trauma.

With reference to FIG. 12, another noncylindrically shaped hole 142 is shown. Rather than forming hole 142 by advancing outlet portion 58 from the epicardium 134 to the endocardium 136 as shown in FIG. 11, hole 142 is formed endovascularly, with outlet portion 58 advancing from the endocardium 136 and into the myocardium 132 a predetermined distance *d*. As mentioned above, to form holes endovascularly, handpiece 54 may be configured as a catheter, with access to the left ventricle of the heart provided through, for example, a femoral artery and the aorta. To form hole 142 with a diameter greater than diameter d_{es} of end surface 60 at the endocardium 136, tissue drill 50 is configured to advance outlet portion 58 relatively slowly at or near the epicardium 136 and then to increase the speed. This results in more tissue being ablated at or near the endocardium 136 than at the "bottom" of hole 142 within the myocardium 132. Laser energy may also be emitted while outlet portion 58 retracts to ablate more tissue toward the endocardium 136. The speed of advancement may be varied by varying either the revolutions per second at which outlet portion 58 rotates or the pitch of threading 76 and/or 78, or both. As mentioned above, rather than varying the speed at which outlet portion 58 advances, the level of emitted laser energy L may be varied. In this regard, to form hole 142, tissue drill 50 may be configured to emit laser energy L at a relatively high level when outlet portion 58 begins to advance, and then to decrease the level as outlet portion 58 advances distance *d*.

Alternatively, rather than adjusting the speed or the energy level, outlet portion 58 may reciprocate a multiple of times either at increasing depths or at decreasing depths. For example, referencing FIG. 12, if the desired depth of the hole to be formed is distance *d* (that is, the distance end surface 60 advances beyond the distal end of handpiece 54), then tissue drill 50 may be configured to advance outlet portion 58 a distance *d* on a first stroke and then to advance outlet portion 58 a distance which incrementally decreases for each subsequent stroke for a predetermined number of strokes. Accordingly, even though the speed at which outlet portion 58 advances and the level at which laser energy L is emitted, hole 142 may be formed with a relatively large diameter at the endocardium 136 and tapered toward the epicardium 134 because tissue toward the endocardium 134 is subject to repeated laser energy with the multiple strokes of outlet portion 58. Therefore, a greater portion of this tissue is ablated because of the increased level of energy received per unit time.

Alternatively, rather than decreasing the distance of the stroke, the distance of each multiple stroke may be incrementally increased to form hole 140 of FIG. 11. In addition, if it is desired to form a hole with a relatively large-diameter inner chamber, then tissue drill 50 may pause outlet portion 58 at a predetermined distance for a predetermined amount of time to concentrate laser energy at one location to ablate a relatively large portion of tissue at that location.

Delivery of Medicament to Tissue

An exemplary system for delivering medicament to tissue which is configured in accordance with the present invention is illustrated in FIG. 13. Exemplary medicament delivery system is referenced with numeral 150 and may be utilized to form a hole or channel in tissue, for example, cardiac tissue (myocardium), and then to deliver medicament, for example, a therapeutic agent for the treatment of cardiovascular disease, or a growth factor, to the tissue by partially or fully filling the hole or channel with the medicament, by injecting medicament into the tissue surrounding the hole or channel, or by administering medicament to a region which includes the hole or channel and the surrounding tissue. This process may be repeated to form and fill a plurality of holes and channels in a targeted area of tissue. In contrast to conventional systemic delivery approaches, the system 150 of the present invention delivers medicament in a controlled manner to specific targeted tissue. The terms *hole* and *channel* used herein indicate any space formed in tissue or through a section of tissue, which space may be substantially regular in shape, such as circular, elliptical, curvilinear, or rectilinear, or substantially irregular in shape.

The exemplary embodiment of delivery system 150 illustrated in FIG. 13 forms the holes or channels by removing tissue with laser ablation. As mentioned above, it has been found that tissue ablation with laser energy stimulates a natural biological process of angiogenesis in the heart. In addition, angiogenic-enhancing growth factors have been found to promote angiogenesis in the heart. Accordingly, a synergistic stimulation and promotion of angiogenesis in the heart is created by augmenting the heart's natural angiogenic response to laser ablation with the delivery of growth factor to those areas of the myocardium which have been ablated. The coupling of the heart's natural response to the formation of channels with the delivery of angiogenic growth factor into or adjacent to those channels provides a benefit to patients not possible prior to the present invention.

Medicament delivery system 150 may include many of the same elements as exemplary tissue drill 50 discussed above. Elements of medicament delivery system 150 which are substantially analogous to elements of tissue drill 50 use like reference numerals with the addition of a prime ('). For example, medicament delivery system 150 includes a handpiece 54' which may be substantially

the same as handpiece 54 of tissue drill 50. This referencing convention will be used in the description hereunder, and the earlier description of such analogous elements will not be repeated in connection with medicament delivery system 150.

In cardiac applications of the system 150 of the invention, the administration of medicament such as endothelial growth factor to cardiac tissue such as myocardium promotes cardiovascular angiogenesis. Growth factors are proteins that stimulate or enhance cell growth. Growth-factor proteins may be packaged in carrier molecules to specifically enhance angiogenesis. For example, the naked DNA of the growth-factor protein may be combined with a cellular matrix. Examples of cellular matrixes include fibrin, plasma, and any other structure that enhances the biocompatibility of the growth factor in the tissue, the angiogenic activity of the growth factor, and/or the sustained release of the growth factor into the tissue. There are many commercially available growth factors that promote angiogenesis, such as vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), transforming growth factor-beta (TGF-β), and platelet-derived growth factor (PDGF). The term *medicament* used herein may include growth factor alone, growth factor in combination with a cellular matrix, or growth factor in combination with any other component that is known to assist in the delivery of the growth factor. In addition, medicament could include any other substance that stimulates angiogenic activity in the heart.

To deliver medicament to myocardium, exemplary medicament delivery system 150 includes a tissue-removal device for forming holes or channels in tissue, such as a source of laser energy and medicament 152 and an ablating and injecting device 154. As discussed in more detail below, ablating and injecting device 154 includes an optical fiber which receives laser energy from source 152 for ablating tissue to form a channel, and a delivery member which receives medicament from source 152 for injection into the channel. In cardiac applications, system 150 is able to deliver growth factor directly into the ischemic myocardium of a patient to promote the growth of endothelial cells.

With additional reference to FIGS. 14 and 15, exemplary ablating and injecting device 154 may include an optical fiber 156 and a delivery member 158 molded together into a unitary structure with cladding 160. As described above, exemplary optical fiber 156 may include a core 82' and a cladding 84', with core 82' having an inlet 86' for receiving laser energy and outlet 62' for emitting laser energy, as indicated by arrow L in FIG. 13. Exemplary delivery member 158 may include a wall 162 in which is defined a lumen 164 with an inlet 166 for receiving medicament and an outlet 168 for providing medicament, which is indicated by arrow M in FIG. 13.

Ablating and injecting device 154 has an end surface 170 and an outlet portion 172. Outlets 62' and 168 may be substantially coplanar with end surface 170.

Referencing FIG. 16, exemplary laser energy and medicament source 152 may include a laser 110', a drive motor 112', a control unit 114', a user interface 116', and a coupler 118' as described above. Source 152 may also include a medicament supply 174 for providing medicament M and an injection unit 176 connected to supply 174, both of which are connected to control unit 114'. A coupler 178 connects lines from laser optics 120' and injection unit 176 into the unitary ablating and injecting device 154.

Analogous to optical fiber 56 described above, exemplary ablating and injecting device 154 is rotatable about an axis of rotation E and translatable between an advanced position and a retracted position. With additional reference to FIGS. 17A and 17B, system 150 may form a channel 138 in myocardium 132, either partially through the myocardium or completely through the myocardium. In accordance with the present invention, as distal portion 172 of ablating and injecting device 154 retracts from the advanced position to the retracted position, as shown by arrow B, control unit 114' activates injection unit 176 to inject medicament M from supply 174 into delivery member 158 and through outlet 168 into channel 138, as shown in FIG. 17A. When device 154 is in the retracted position and handpiece 54' is moved away, a discrete amount 179 of medicament is left within channel 138, as shown in FIG. 17B. The discrete amount 179 may partially or fully fill channel 138. The procedure may be repeated a plurality of times at different locations in the myocardium 132, thereby seeding the myocardium with medicament such as angiogenesis-promoting growth factor. Exemplary injection unit 176 may inject medicament through the use of hydraulics, pneumatics, aerosol, or other means.

In addition, injection unit 176 may be configured as an injection jet nozzle which utilizes high pressure to create a fluid column of medicament for injection into tissue. A jet injector may also be used to form a hole in or through tissue with high-pressure fluid (which may contain medicament), either by tearing (or expanding) the tissue or by removing the tissue, or a combination of both. The jet injector may be configured to deliver medicament to the tissue while forming the hole or channel therein.

Regarding the coupling of ablating and injecting device 154 to laser energy and medicament source 152, reference is made to FIGS. 18 and 19 in which an exemplary embodiment of a coupling assembly 180 is illustrated. Exemplary coupling assembly 180 includes a housing 182 which is adapted to receive a reel 184 in a rotatable and sealed

relationship. Reel 184 includes a passage 186 formed axially therethrough in which ablating and injecting device 154 is securely received. Reel 184 also includes an annular channel 188 and a through hole 190 extending between passage 186 and channel 188. Delivery member 158 extends from device 154 into through hole 190 to be in communication with channel 188. A feeding tube 192 extends between a port 194 of housing 182 and the medicament injection and supply units 176 and 174.

A plurality of O-rings 196 may be used to seal reel 184 within housing 182, device 154 within passage 186, and delivery member 158 within through hole 190. Rings 196 may be low-friction Teflon® seals. Specialized couplings, such as a Touhy-Borst valve coupling, may be used to connect device 154 to reel 184. Housing 182 may include structure such as stops to limit the axial translation of reel 184. Although exaggerated in the drawings, tolerances between reel 184 and housing 182 may be on the order of less than about 0.005 inch. In addition, housing 182 may be of a two-piece design with two halves hinged together to allow easy access to the inside of the housing.

Coupling assembly 180 allows ablating and injecting device 154 to rotate about rotational axis E under power from drive unit 112' while receiving laser energy and medicament. For example, device 154 may be driven about 40 revolutions in one direction (yielding the advanced position), and then driven about 40 revolutions in the other direction (yielding the retracted position). Because of the secure coupling with device 154, reel 184 is driven by device 154 to rotate about axis E, that is device 154 may act as a drive shaft. When it is desired to deliver medicament to tissue, injection unit 176 injects medicament through tube 192 (which is indicated by arrow M) and into a space 198 defined within channel 188 and between reel 184 and housing 182. Medicament is accordingly urged and/or injected into the lumen 164 of delivery member 158. Medicament may be continuously injected into delivery lumen 158 while reel 184 rotates. As described above, the injection of medicament into delivery lumen 158 may be limited to when device 154 is retracting.

With general reference to FIG. 13, rather than coupling delivery member 158 to medicament supply 174 at source system 152, exemplary handpiece 54' may include an assembly for injecting medicament into delivery member 158 (not shown). For example, a pressure capsule, such as a CO_2 capsule, may inject medicament into the inlet 166 of lumen 164 and out of the outlet 168. Delivery member 158 may be coiled within handpiece 54' when in the retracted positioned, and may then uncoil while being driven to the advanced position. In the embodiment with an injection assembly at

handpiece 54', delivery member 158 may have a relatively short overall length as the handpiece is positioned at or near the tissue targeted to receive medicament.

Alternative configurations of the ablating and injecting device of the present invention are shown in FIGS. 20 and 21. Referencing FIG. 20, exemplary ablating and injecting device 154' includes an optical fiber 156' and a delivery member 158' molded together into a unitary structure with cladding 160'. Exemplary delivery member 158' may be crescent shaped in cross-section, as shown. As discussed above, the diameter d_o of the outlet of optical fiber 156' is preferably at least one half of the diameter d_{es} of the end surface 170' of device 154'. For example, diameter d_o may be about 0.6 mm and diameter d_{es} may be about 1.0 mm. Accordingly, as device 154' rotates about axis E, laser energy emitted from optical fiber 156' ablates tissue along the entire radial sweep of axis E, thereby forming a channel of about 1.0 mm in diameter, which is described above (see FIG. 8).

Referencing FIG. 21, exemplary ablating and injecting device 154" includes a pair of optical fibers 156*a* and 156*b* and a delivery member 158" molded together into a unitary structure with cladding 160". Exemplary delivery member 158" may be rectilinear shaped in cross-section, as shown. The outlet of each optical fiber 156 preferably has a diameter d_o of approximately one quarter of the diameter d_{es} of the end surface 170" of device 154'. Therefore, collectively the diameters d_o of the optical fibers 156*a* and 156*b* comprise about one half of the diameter d_{es} of the end surface 170". For example, diameter d_o may be about 0.3 mm and diameter d_{es} of end surface 170" may be about 1.0 mm. Alternatively, any number of fibers may be used in multiple-fiber device 154", such as four 0.15-mm diameter fibers.

Optical fiber becomes more flexible when its diameter is reduced. It follows that the pair of optical fibers 156*a* and 156*b* of FIG. 21 each with a diameter of about 0.3 mm are more flexible than the single optical fiber 156' of FIG. 20 with a diameter of about 0.6 mm. As such, device 154" is more flexible and is able to follow a more tortuous path than device 154'. Accordingly, device 154' shown in FIG. 20 is useful in direct-visualization procedures in conjunction with a handpiece as described above, such as in intra-operative or trans-thoracic procedures, which do not require the optical fiber to bend through tortuous paths. Device 154" shown in FIG. 21 is useful in indirect-visualization procedures in conjunction with a catheter and a scope, such as trans-septal and endovascular procedures. For example, device 154" may be inserted into a femoral artery, through the aortic arch, and into the left ventricle to ablate tissue from the endocardium to the epicardium.

Rather than forming channels in tissue with laser ablation as described above, tissue may be removed to form channels in accordance with the present invention for medicament delivery by other methods, for example, by high-frequency electrical energy or radio-frequency (RF) energy. Referencing FIG. 22, an exemplary embodiment of a tissue-removal and medicament-delivery device 200 which uses electrical energy to remove tissue in accordance with the present invention is illustrated. Device 200 includes an electrode 202 disposed on a distal tip of the device, an insulator 204 proximal to the electrode 202, and a body 206. A delivery lumen 208 is formed axially through electrode 202, insulator 204, and body 206, and has an outlet 210 in a distal end of device 200.

An alternative embodiment of an electrical-energy tissue-removal and medicament-delivery device 200' of the invention is illustrated in FIG. 23. Rather than having an axial delivery lumen, device 200' includes at least one delivery lumen 210 formed longitudinally through at least the body 206'. As shown in FIG. 23, two delivery lumens 212*a* and 212*b* are formed through the body 206' and extend into the insulator 204'. Each lumen 212 has an outlet 214 formed on a side 216 of device 200'. In the exemplary embodiment, outlets 214*a* and 214*b* may be substantially diametrically opposed within the device. Alternatively, each lumen 212 may have a plurality of outlets which form an array of ports on the side 216 of device 200'.

With additional reference to FIG. 24, in use, the tissue-removal and medicament-delivery devices 200 and 200' generate high-frequency electrical energy, which in turn generates an ionized plasma corona 216 and converts tissue 132 to gas to create a channel or hole in the tissue. A ground plate 218 may be provided such that tissue 132 is positioned between the ground plate and electrode 202. The ground plate 218 may be used to control conduction paths (shown by the dashed arrows) formed by the positively charged electrode 202, which controls the formation of channels in tissue. After holes or channels are formed in tissue, medicament such as growth factor that promotes angiogenesis may be delivered to the tissue within the hole or channel itself via the delivery lumen as described above. Alternatively, with reference to FIG. 25, medicament may be delivered into the walls of the hole or channel 138 and into the tissue 132 surrounding the hole or channel 138 via the delivery lumens 212, as indicated by arrows M.

Referencing FIG. 26, another exemplary embodiment of an electrical-energy tissue-removal and medicament-delivery device 200" of the invention is illustrated. Device 200" includes a cathode 220 disposed on a distal tip of the device, an insulator 204" proximal to the electrode 202, an anode 222 proximal to the insulator, and a body 206". A delivery lumen 208

is formed axially through the device 200". Electrical-conducting leads (not shown) connect the cathode and anode 220 and 222 to a power source. When activated, conduction paths (shown in dashed lines) between the cathode 220 and the anode 220 define the ionized plasma cornea 216' which converts tissue to gas to form channels.

Another exemplary embodiment of a medicament-delivery system 230 of the present invention is illustrated in FIGS. 27, 28, and 29. System 230 includes an ablating and injecting device 232 received within a catheter 234. Exemplary ablating and injecting device 232 includes a pair of optical fibers 236*a* and 236*b* and a pair of delivery members 238*a* and 238*b*. Cladding 240 configures the fibers 236 and 238 into a unitary and cylindrical device. Optical fibers 236 and delivery members 238 may be configured and function in accordance with the description provided above. Exemplary device 232 also includes rifling tracks 242 formed on an annular lip 244 thereof, preferably at a distal end of the device, and exemplary catheter 234 includes rifling 246 formed on an inner surface thereof for slidingly engaging with the rifling tracks 242 of the ablating and injecting device 232. Accordingly, as ablating and injecting device 232 rotates, the rifling 246 translates the device 232 axially within catheter 234, between the advanced and retracted positions as described above.

Exemplary medicament-delivery system 230 is particularly useful in endovascular procedures which may entail guiding the ablating and injecting device 232 and catheter 234 through tortuous paths to its final destination. Accordingly, it is preferable to maximize as much as possible the flexibility of the ablating and injecting device 232. As such, it is preferable for the diameters of the optical fibers 236 to be as small as possible while still capable of carrying sufficient laser energy to ablate tissue. In a preferred embodiment, the diameter of each optical fiber 236 may be about 0.25 mm. The overall diameter of the device 232 may then be about 0.5 mm.

In an alternative embodiment of the ablating and injecting device of the present invention, the medicament may be delivered directly to the tissue surrounding the channel instead of delivering the medicament into the channel or into the tissue by way of the channel. This may be advantageous where it is desirable to avoid systemic administration of the medicament, which could occur through washout of medicament when it is delivered directly into the channel. Various configurations of this alternate embodiment are shown in FIGS. 30-40.

Referencing FIG. 30, alternate head portion 100' has one or more needles 250 on the outer rim of its tissue-engaging surface for penetrating the tissue around the perimeter of the tissue channel opening. This provides access directly to the tissue surrounding the channel. The delivery device is provided with one or more medicament lumens 164' which are in fluid communication with needles 250. Needles 250 pierce the tissue around the perimeter of the channel opening and deliver medicament by way of lumen or lumens 164'. The medicament diffuses through the tissue without having to enter into the channel, thus avoiding medicament washout and the possibility of systemic delivery of the medicament. FIG. 31 illustrates the end surface of head portion 100' having an array of needles 250 around its perimeter. FIG. 32 illustrates medicament 252 diffusing into the tissue surrounding channel 138. Other embodiments of alternate head portion 100' are illustrated in FIGS. 33 and 34. FIG. 33 illustrates head portion 100' having a nozzle or nozzles 254 around its perimeter. Nozzles 254 are adapted to atomize the medicament when head portion 100' is placed up against the tissue surrounding the channel opening. As in the previous embodiment using needles 250, the medicament is diffused directly into the tissue and not into the channel where it can be washed out into the patient's system. FIG. 34 illustrates yet another embodiment wherein head portion 100' has a port or ports 256 on the head portion perimeter for diffusing medicament directly into the tissue surrounding the channel opening.

FIGS. 35 and 36 illustrate that medicament can be provided to head portion 100' through a single lumen 164" which is in fluid communication with an annular manifold 258 which communicates through the perimeter of head portion 100' to ports 256. FIG. 37 illustrates an alternate embodiment wherein single lumen 164" has an annular geometry. Those skilled in the art will appreciate that this single lumen embodiment incorporating manifold 258 can also be utilized with nozzles 254 or needles 250. Similarly, it will be appreciated by those skilled in the art that other means for diffusing medicament directly into the tissue surrounding the channel opening can be utilized for like effect.

FIG. 38 illustrates yet another exemplary embodiment wherein at least one delivery lumen 264 is in fluid communication with delivery outlet 266 and at least one vacuum lumen 268 is in communication with a vacuum source (not shown) and terminates in vacuum outlet 270. By providing a vacuum to head portion 100' through lumen 268 to outlet 270 the clinician can insure that medicament can be delivered directly to the tissue through lumen 264 and outlet 266. It will be appreciated by those skilled in the art that this embodiment could include a

plurality of vacuum lumens and a plurality of delivery lumens to maximize the effectiveness of the invention.

Referencing FIG. 39, an alternate exemplary embodiment of an electrical-energy tissue-removal and medicament-delivery device 200" is illustrated wherein the medicament can be directly delivered into the tissue walls and diffused into the tissue surrounding the channel. As in the embodiment of FIG. 23, two delivery lumens 212a' and 212b' are provided, each having its respective outlet 214a' and 214b'. In the exemplary embodiment, outlets 214a' and 214b' may be substantially diametrically opposed within the device. In this embodiment, vacuum lumens 212c' and 212d' are provided longitudinally through the body of device 200" and in communication with outlets 214c' and 214d', respectively. Outlets 214c' and 214d' may also be diametrically opposed to each other. Vacuum lumens 212c' and 212d' are in communication with a vacuum source (not shown) which provides a vacuum through lumens 212c' and 212d' to outlets 214c' and 214d' to draw the tissue channel wall up against outlets 214c' and 214d'. Due to their proximity, sufficient vacuum can be provided to also draw the tissue wall up against outlets 214a' and 214b'. Medicament 252 can then be provided through delivery lumens 212a' and 212b' to outlets 214a' and 214b' and directly into the tissue wall of the channel as illustrated in FIG. 40. In the embodiment shown, outlets 214a' and 214b' are distal to outlets 214c' and 214d'. However, it is also possible to configure the outlets so that 214c' and 214d' outlets are distal to 214a' and 214b' outlets and to configure the delivery and vacuum lumens accordingly. As is the case with the embodiment of FIGS. 30-38, this embodiment also permits medicament to be diffused into the tissue surrounding the channel without having systemic washout of the medicament.

In addition to removing tissue to form holes or channels by laser ablation or by high-frequency electrical energy, holes or channels may be formed in tissue mechanically with hot tips or biopsy needles, ultrasonically, or hydraulically with high-pressure water. The medicament can be growth factor, which may take many forms. For example, growth factor may be delivered as a protein solution. Alternatively, growth factor may be combined with a fibrin, collagen, or plasma to form a cellular matrix gel. Growth factor may also be mixed into a semi-solid using a biocompatible matrix. Further, growth factor may be delivered to tissue in an atomized form under pressure. The medicament can also be a gene that encodes for said growth factor, or any other therapeutic agent or gene therapy agent that promotes angiogenesis or any therapeutic agent for the treatment of cardiovascular disease. Whatever the form may be, the angiogenesis-promoting

growth-factor solution is administered through the delivery lumen(s) to enhance and accelerate the angiogenic process. The growth factor solution may be driven into the channel and/or tissue using, for example, a pneumatic system, a mechanical system (e.g., a syringe-type system with a plunger), a hydraulic system (e.g., using fluids or gas), or a gravitational system.

Those skilled in the art will understand that the embodiments of the present invention described above exemplify the present invention and do not limit the scope of the invention to these specifically illustrated and described embodiments. The scope of the invention is determined by the terms of the appended claims and their legal equivalents, rather than by the described examples. In addition, the exemplary embodiments provide a foundation from which numerous alternatives and modifications may be made, which alternatives and modifications are also within the scope of the present invention as defined in the appended claims.

CLAIMS

What is claimed is:

1. A medicament delivery system comprising:

A) a laser source for providing laser energy;

B) a medicament source for providing medicament;

C) an ablating and delivering device including:

(1) an optical fiber having:

(a) a distal portion;

(b) an inlet end for coupling to said laser source; and

(c) an outlet end disposed at said distal portion for emitting laser energy; and

(2) a delivery member having:

(a) a lumen;

(b) a distal portion;

(c) an inlet end for coupling to said medicament source; and

(d) an outlet end disposed at said distal portion for injecting medicament; and

D) a handpiece which receives said ablating and injecting device in controlled, movable relationship thereto.

2. A medicament delivery system as claimed in claim 1 wherein said ablating and injecting device further includes cladding disposed about said distal portions of said optical fiber and said delivery member, thereby forming an integral distal portion of said ablating and delivering device.

3. A medicament delivery system as claimed in claim 2 wherein said handpiece reciprocates said distal portion of said ablating and injecting device between an advanced position and a retracted position.

4. A medicament delivery system as claimed in claim 3 further comprising a control unit connected to said laser source and said medicament source.

5. A medicament delivery system as claimed in claim 4 wherein said control unit activates said laser source to emit laser energy when said distal portion of said ablating and injecting device moves from said retracted position to said advanced position.

6. A medicament delivery system as claimed in claim 5 wherein said control unit activates said medicament source to inject medicament when said distal portion of said ablating and injecting device moves from said advanced position to said retracted position.

7. Apparatus for use in delivering medicament to tissue, comprising:
an ablating and delivering device including:
(1) an optical fiber having:
(a) a distal portion;
(b) an inlet end for coupling to a laser energy source; and
(c) an outlet end disposed at said distal portion for emitting laser energy; and
(2) a delivery member having:
(a) a lumen;
(b) a distal portion;
(c) an inlet end for coupling to a medicament source; and
(d) an outlet end disposed at said distal portion for providing medicament.

8. Apparatus as claimed in claim 7 further comprising a handpiece which receives said ablating and delivering device in controlled, movable relationship thereto.

9. A method for delivering medicament to tissue, said method comprising the steps of:
providing access to the tissue;
forming a channel in the tissue by removing tissue; and
providing medicament in said channel and/or in tissue surrounding said channel.

10. A method as claimed in claim 9 wherein said forming step comprises the step of:
ablating the tissue with laser energy.

11. A method as claimed in claim 9 wherein said forming step comprises the step of:
converting the tissue to gas with high-frequency electrical energy.

12. A method as claimed in claim 9 wherein said step of providing medicament comprises the step of:

providing growth factor.

13. A method as claimed in claim 12 wherein said step of providing growth factor comprises the step of:

providing growth factor combined with a cellular matrix.

14. A method as claimed in claim 12 wherein said step of providing growth factor comprises the step of:

providing growth factor combined with fibrin.

15. A method as claimed in claim 12 wherein said step of providing growth factor comprises the step of:

providing growth factor combined with collagen.

16. A method as claimed in claim 12 wherein said step of providing growth factor comprises the step of:

providing growth factor in an atomized form.

17. A method as claimed in claim 9 wherein said step of providing medicament comprises the step of:

providing medicament pneumatically.

18. A method as claimed in claim 9 wherein said step of providing medicament comprises the step of:

providing medicament hydraulically.

19. A method as claimed in claim 9 wherein the tissue is myocardium;

said forming step comprising the step of forming a channel completely through the myocardium.

20. A method as claimed in claim 9 wherein the tissue is myocardium;

said forming step comprising the step of forming a channel partially through the myocardium.

21. A method as claimed in claim 9 wherein said step of providing a medicament comprises the step of:

providing a medicament to tissue surrounding said channel.

22. A system for delivering medicament to tissue, comprising:

a tissue-removal device for forming a channel in the tissue;

a delivery member for delivering medicament to and/or adjacent to said channel, said delivery member including a lumen with an inlet for receiving medicament and an outlet for providing medicament; and

a handpiece that receives said delivery member so that said outlet is positionable to deliver medicament to said channel.

23. A system as claimed in claim 22 wherein said tissue-removal device includes an optical fiber.

24. A system as claimed in claim 22 wherein said tissue-removal device includes an electrode for emitting high-frequency electrical energy.

25. A system as claimed in claim 22 further including cladding for forming said tissue-removal device and said delivery member into a substantially unitary structure.

26. A system for delivering medicament to tissue, comprising:

a tissue-removing mechanism which removes tissue to form a channel in the tissue; and

a delivery conduit mechanism which moves medicament from a source to said channel.

27. A system as claimed in claim 26 wherein said tissue-removing mechanism removes tissue with laser energy.

28. A system as claimed in claim 26 wherein said tissue-removing mechanism removes tissue with electrical energy.

29. A system as claimed in claim 26 wherein said delivery conduit mechanism includes a lumen with an inlet for receiving medicament from a source and an outlet for providing medicament to said channel.

30. A method for delivering medicament to tissue, said method comprising the steps of:
selecting tissue to receive medicament;
accessing the selected tissue;
stimulating a natural response in the selected tissue; and
providing medicament to the selected tissue.

31. A method as claimed in claim 30 wherein said selecting step comprises the step of:
selecting cardiac tissue.

32. A method as claimed in claim 31 wherein said selecting step comprises the step of:
selecting ischemic cardiac tissue.

33. A method as claimed in claim 32 wherein said stimulating step comprises the step of:
stimulating an angiogenic response in the ischemic cardiac tissue.

34. A method as claimed in claim 33 wherein said providing step comprises the step of:
providing growth factor to the cardiac tissue.

35. A method as claimed in claim 31 wherein said stimulating step comprises the step of:
ablating the selected tissue with laser energy.

36. A method as claimed in claim 35 wherein said ablating step comprises the step of:
ablating the selected tissue to form a hole or channel therein.

37. A method as claimed in claim 36 wherein said providing step comprises the step of:
providing medicament to said hole or channel.

38. A method as claimed in claim 36 wherein said providing step comprises the step of:
providing medicament to tissue surrounding said hole or channel.

39. A method as claimed in claim 31 wherein said stimulating step comprises the step of:
subjecting the selected tissue to high-frequency electrical energy.

40. A method as claimed in claim 31 wherein said providing step comprises the step of:
providing growth factor.

41. A medicament delivery system comprising:
an energy source for providing energy to remove tissue;
a medicament source for providing medicament to the tissue;
an energy transmitting member having a an inlet end for coupling to said energy source and an outlet end disposed at a distal portion for emitting energy;
a medicament delivery member having:
an inlet end for coupling to said medicament source;
at least one lumen through said delivery member for delivering medicament;
a distal portion terminating in a tissue-engaging surface having ports in fluid communication with said lumen for injecting medicament directly into the tissue; and
a handpiece which receives said energy transmitting member and said medicament delivery member.

42. The medicament delivery system of claim 41 wherein said tissue-engaging surface further comprises one or more needles in fluid communication with said lumen for piercing the tissue and injecting medicament directly into the tissue.

43. The medicament delivery system of claim 41 wherein said tissue-engaging surface further comprises one or more nozzles in fluid communication with said lumen for injecting medicament directly into the tissue.

44. The medicament delivery system of claim 41 wherein said energy source comprises a source of laser energy and said energy transmitting member comprises an optical fiber.

45. The medicament delivery system of claim 41 wherein said energy transmitting member comprises an electrode for emitting high-frequency electrical energy.

46. A medicament delivery system comprising:

an energy source for providing energy to remove tissue;

a medicament source for providing medicament to the tissue;

a vacuum source for providing vacuum to the system; and

an energy transmitting and medicament delivery member having a an inlet end for coupling to said energy source, said medicament source and said vacuum source and an outlet end disposed at a distal portion for emitting energy and delivering medicament;

said energy transmitting and medicament delivery member further comprising:

at least a first vacuum lumen in communication with said vacuum source and at least a first medicament delivery lumen in fluid communication with said medicament source; and

at least two ports proximal to said distal portion and in close proximity to each other, comprising at least a first vacuum port in fluid communication with said vacuum lumen for providing vacuum to the tissue and at least a first delivery port is in fluid communication with said medicament delivery lumen for injecting medicament directly into the tissue.

47. The medicament delivery system of claim 46 further comprising:

a second vacuum lumen in communication with said vacuum source;

a second medicament delivery lumen in fluid communication with said medicament source;

a second vacuum port in fluid communication with said second vacuum lumen for providing vacuum to the tissue; and

a second delivery port in fluid communication with said medicament delivery lumen for injecting medicament directly into the tissue.

48. The medicament delivery system of claim 47 wherein said delivery ports are substantially diametrically opposed to each other on the delivery member.

49. The medicament delivery system of claim 47 wherein said vacuum ports are substantially diametrically opposed to each other on the delivery member.

50. The medicament delivery system of claim 46 wherein said energy transmitting and medicament delivery member further comprises a distal portion having a tissue-engaging surface wherein said lumens and said ports terminate for providing vacuum and medicament delivery to the tissue.

51. A medicament injection unit comprising:

an injection jet nozzle;

a medicament source for providing medicament to the tissue and in fluid communication with said nozzle; and

a pressure source in fluid communication with said nozzle and said medicament source.

52. A method of delivering medicament to tissue, said method comprising the steps of;

providing an injection jet nozzle coupled to a source of fluid and coupled to a source of medicament;

delivering said fluid through said nozzle with sufficient pressure to form a hole in or through the tissue;

providing a source of high pressure between said source of medicament and said jet nozzle to create a fluid column of medicament for injection into the tissues; and

delivering medicament to the tissue through said jet nozzle.

53. ; A method of delivering medicament to tissue, said method comprising the steps of;

providing an injection jet nozzle coupled to a source of fluid and coupled to a source of medicament;

providing a source of high pressure between said source of medicament and said jet nozzle to create a fluid column of medicament for injection into the tissues;

delivering said fluid through said nozzle with sufficient pressure to form a hole in or through the tissue while delivering medicament to the tissue through said jet nozzle to the tissue.

54. A method of delivering medicament to tissue, said method comprising the steps of:

providing access to the tissue;

forming a channel in the tissue by removing tissue; and

providing medicament directly to the tissue surrounding said channel.

55. The method of claim 54 further comprising the step of providing medicament directly to the tissue surrounding the opening of the channel.

56. The method of claim 55 further comprising the step of piercing the tissue surrounding the opening of the channels and injecting medicament into the tissue.

57. The method of claim 54 further comprising the step of providing medicament directly to the tissue surrounding said by delivering medicament directly to the tissue comprising the channel wall.

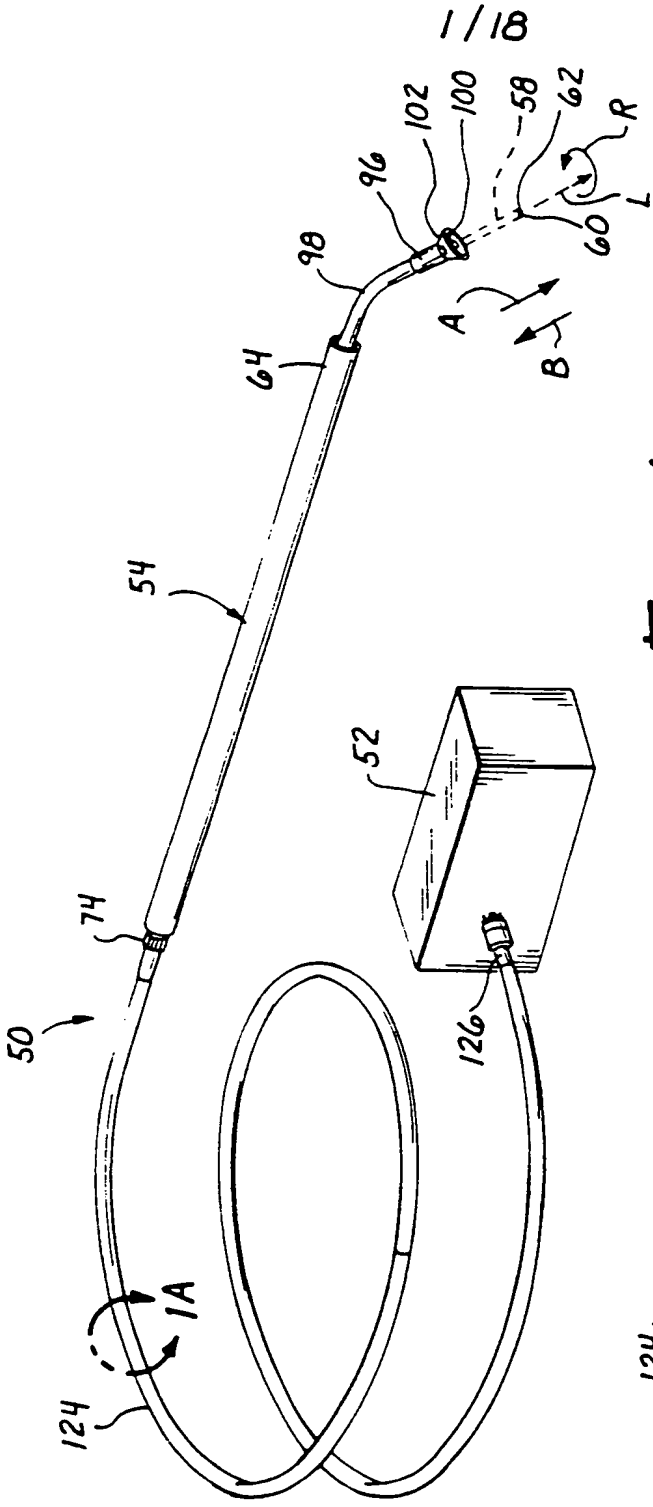


Fig. 1

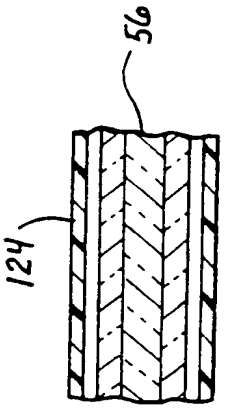


Fig. 1A

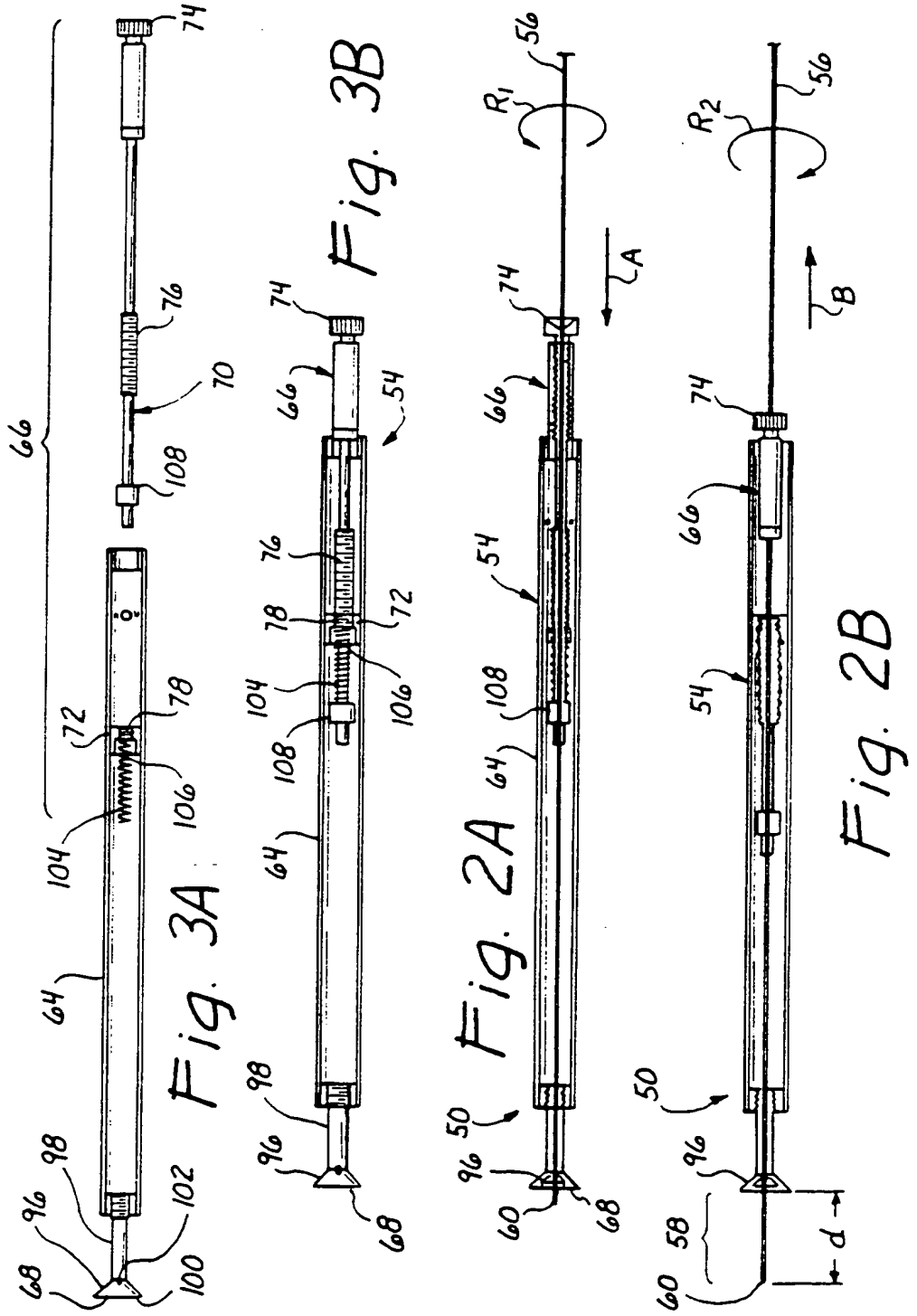


Fig. 3A

Fig. 3B

Fig. 2A

Fig. 2B

Fig. 4

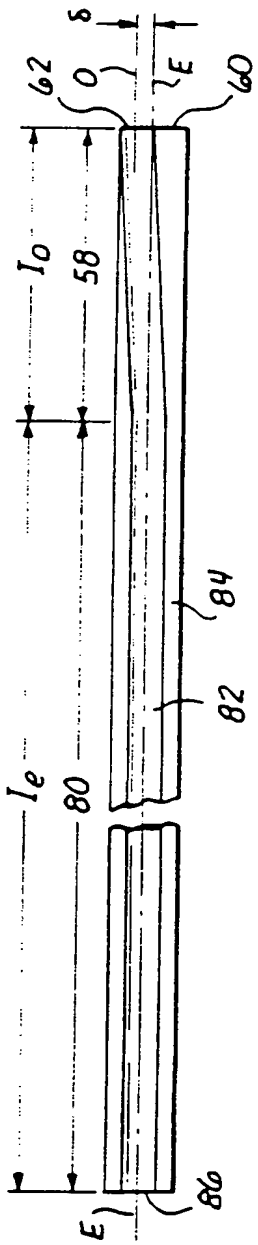


Fig. 6

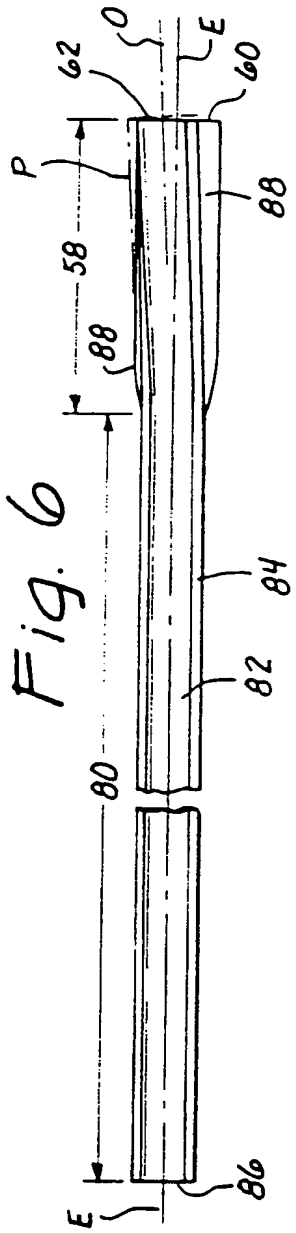


Fig. 7

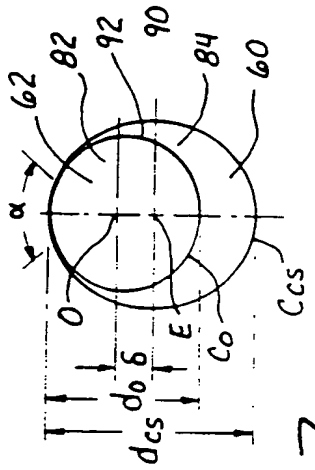
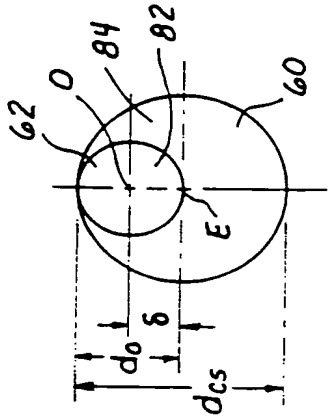


Fig. 5



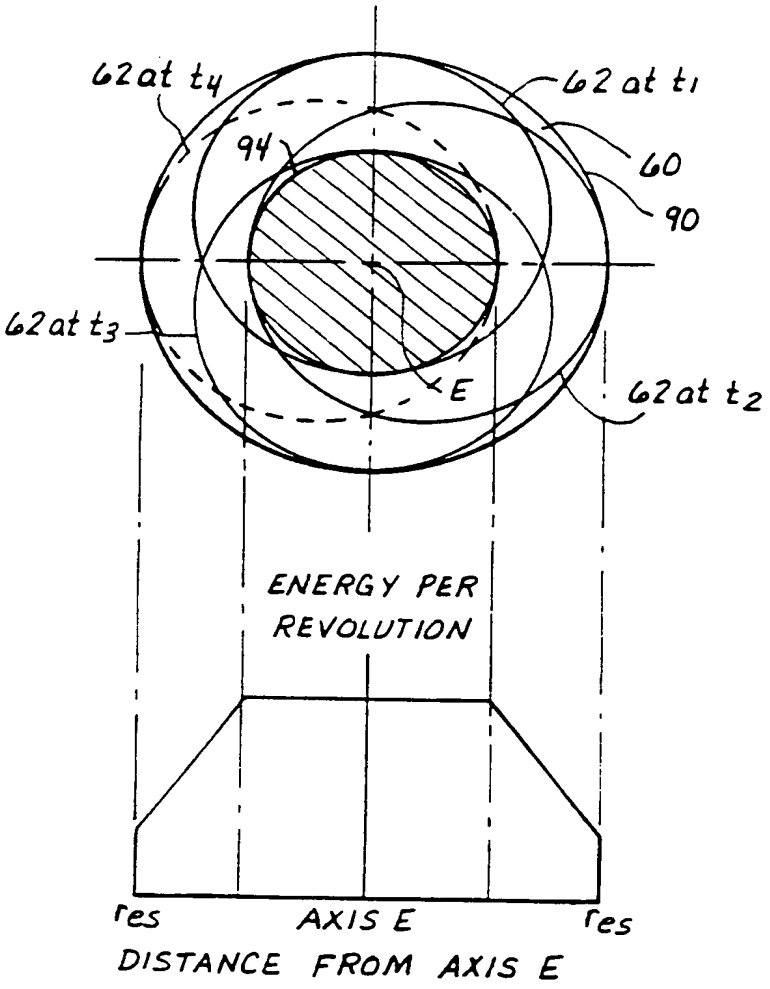


Fig. 8

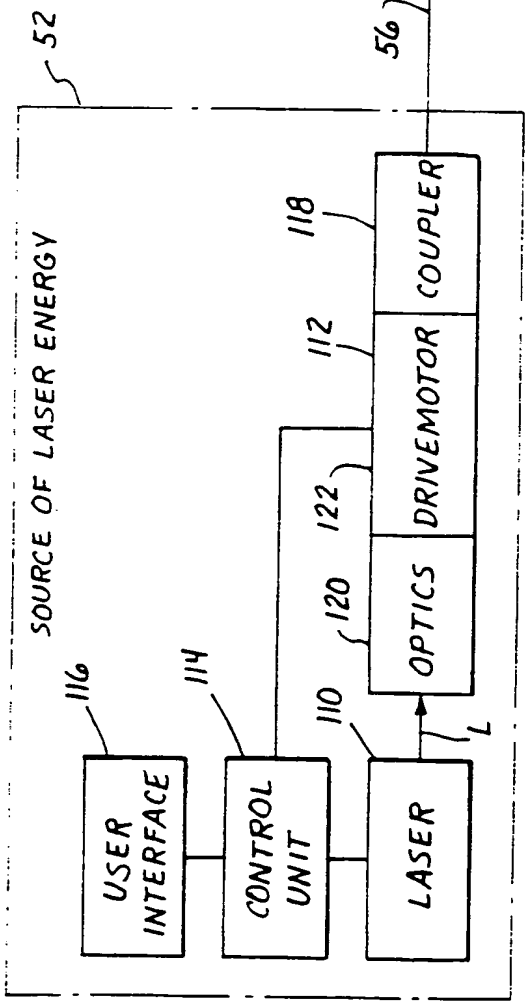


Fig. 9

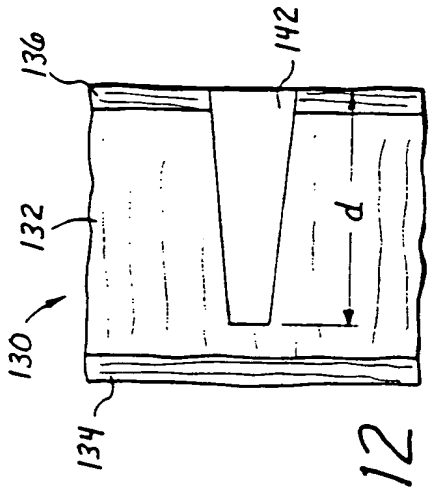


Fig. 12

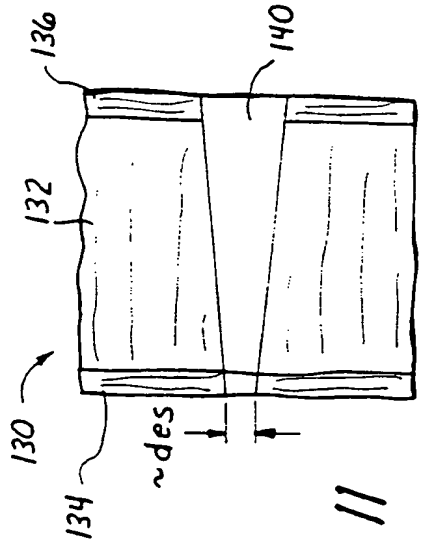


Fig. 11

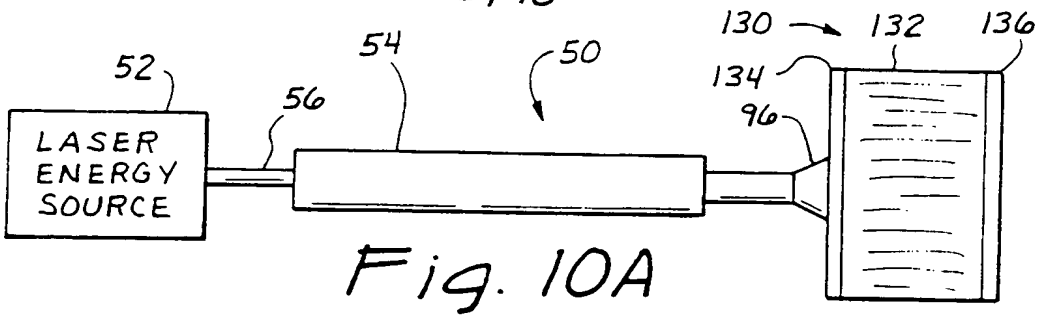


Fig. 10A

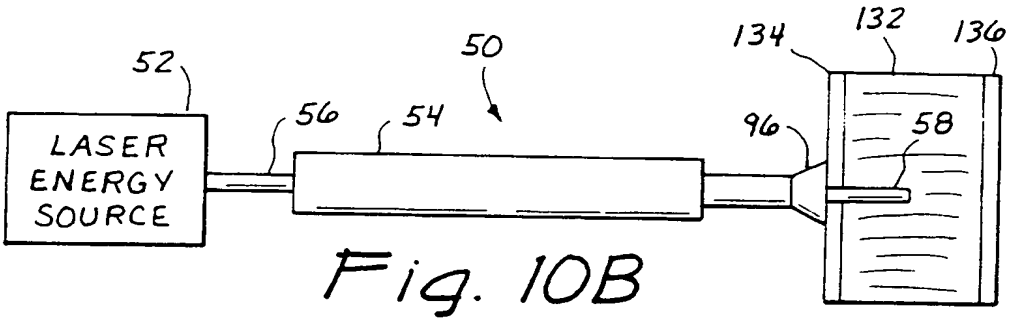


Fig. 10B

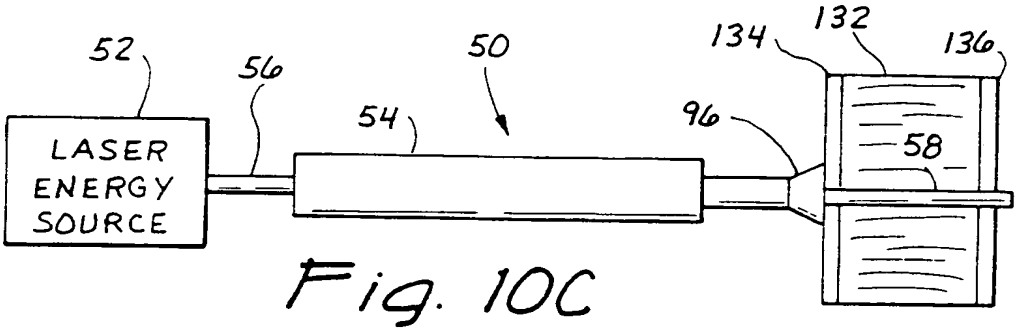


Fig. 10C

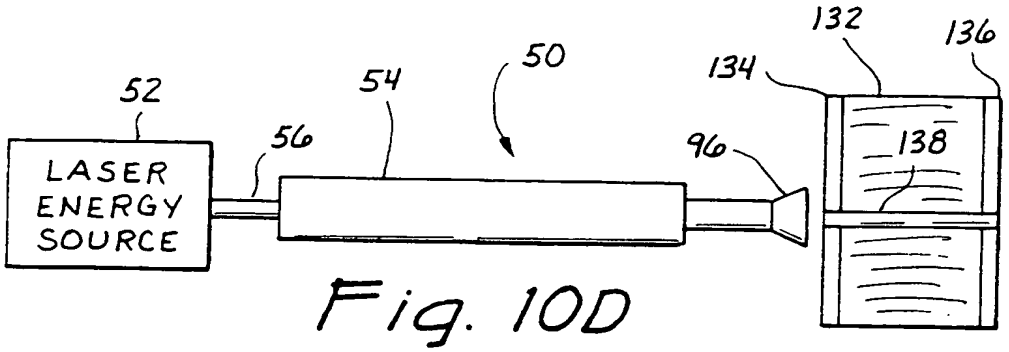


Fig. 10D

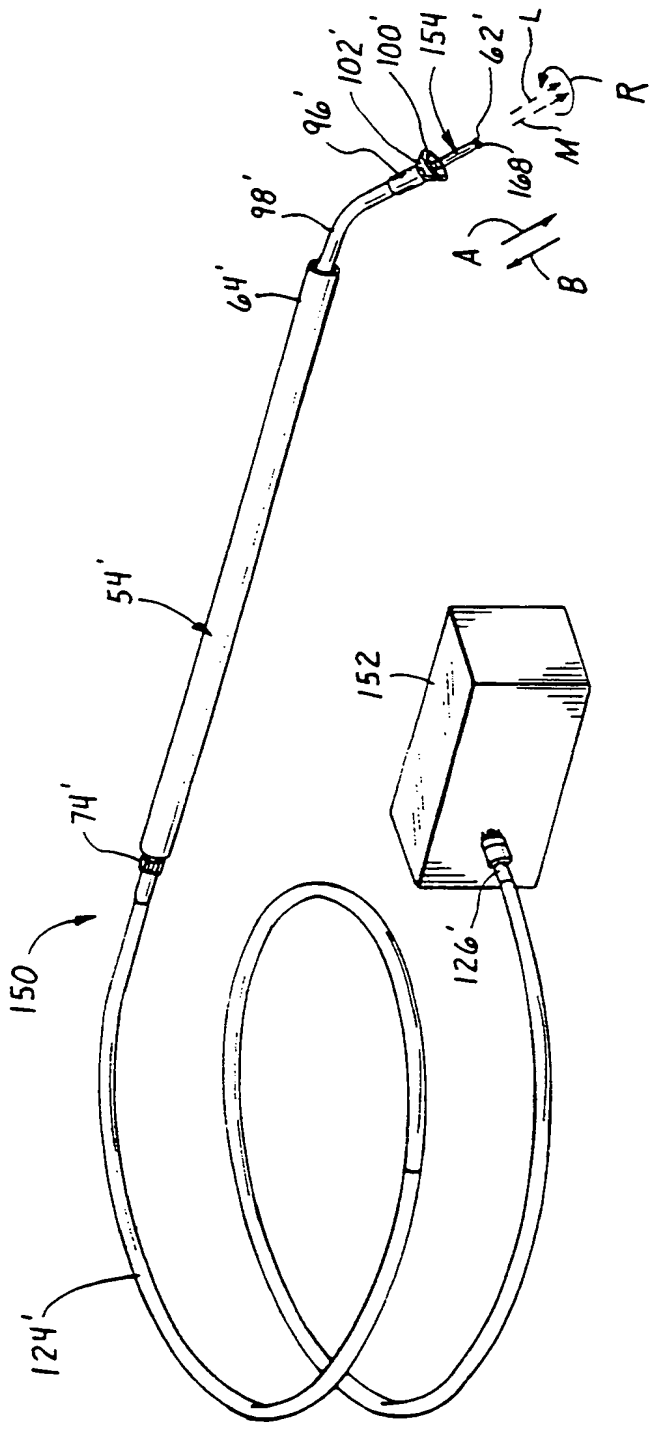


Fig. 13

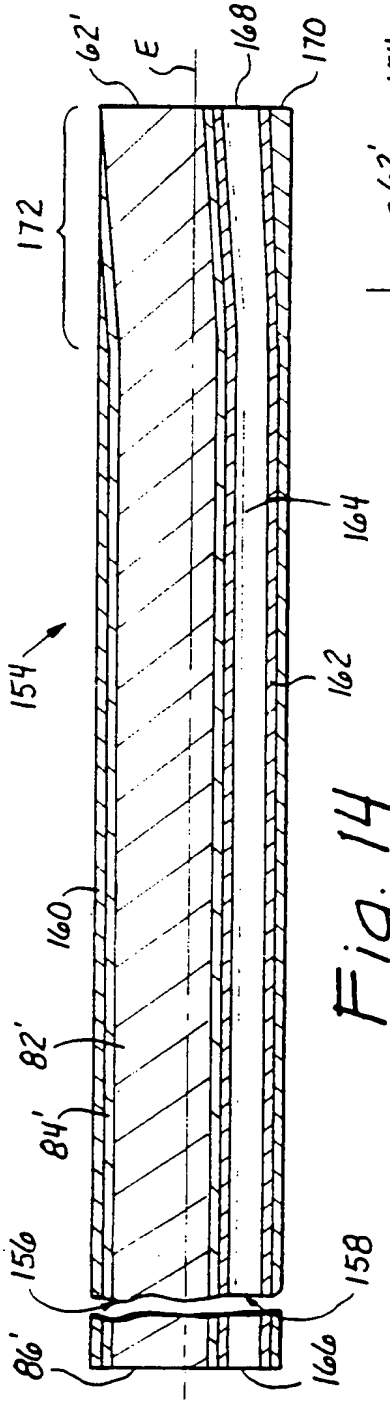


Fig. 14

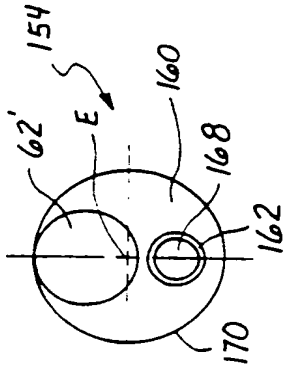


Fig. 15

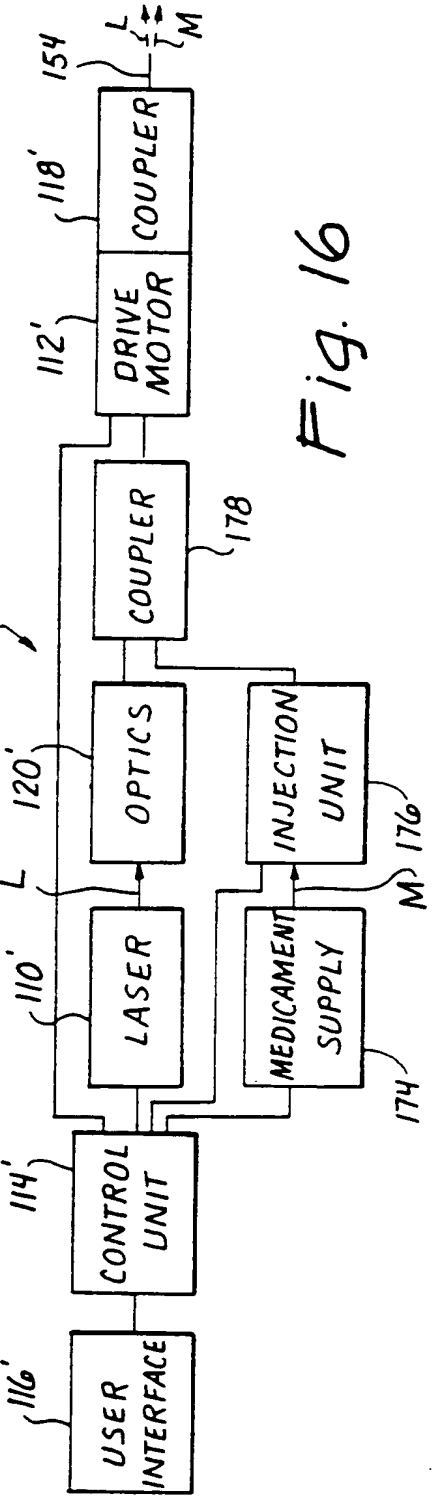


Fig. 16

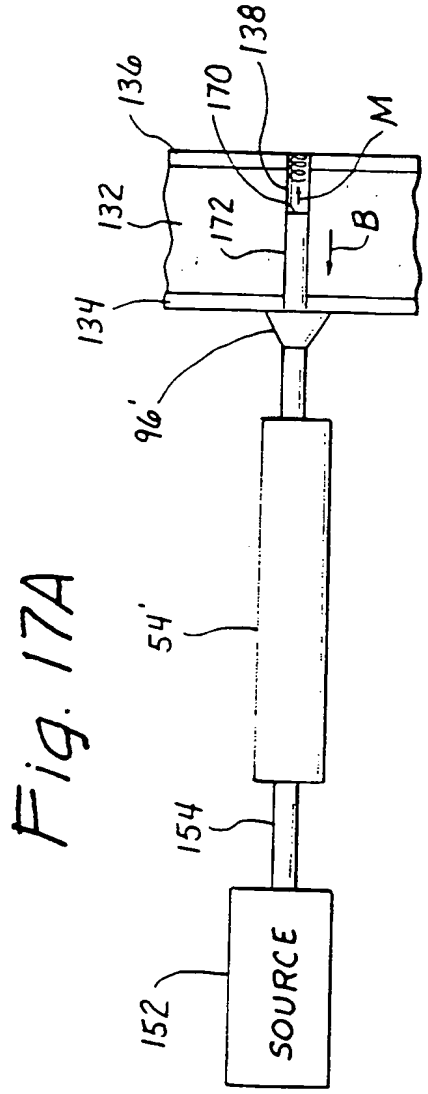


Fig. 17A

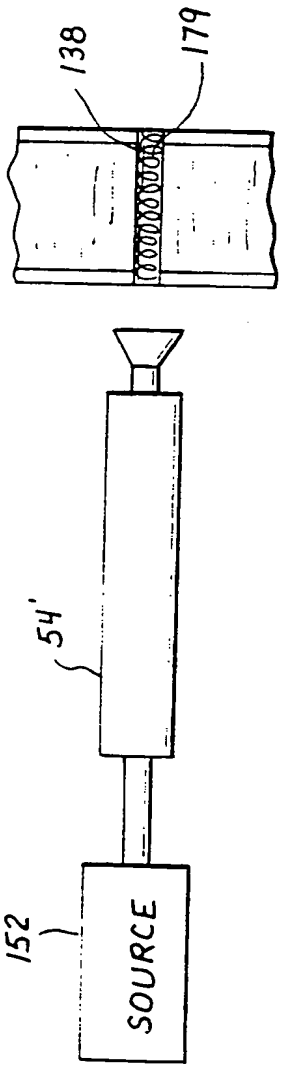
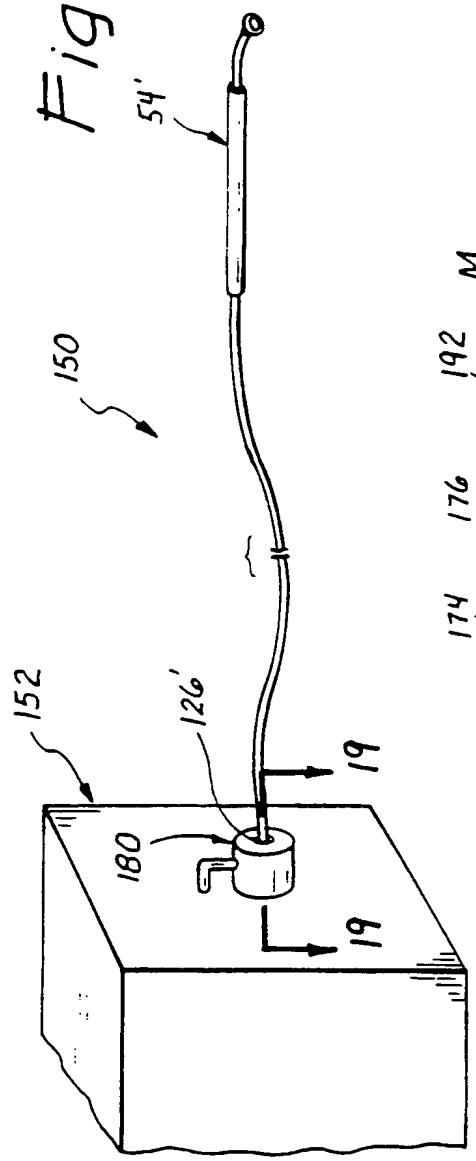


Fig. 17B

Fig. 18



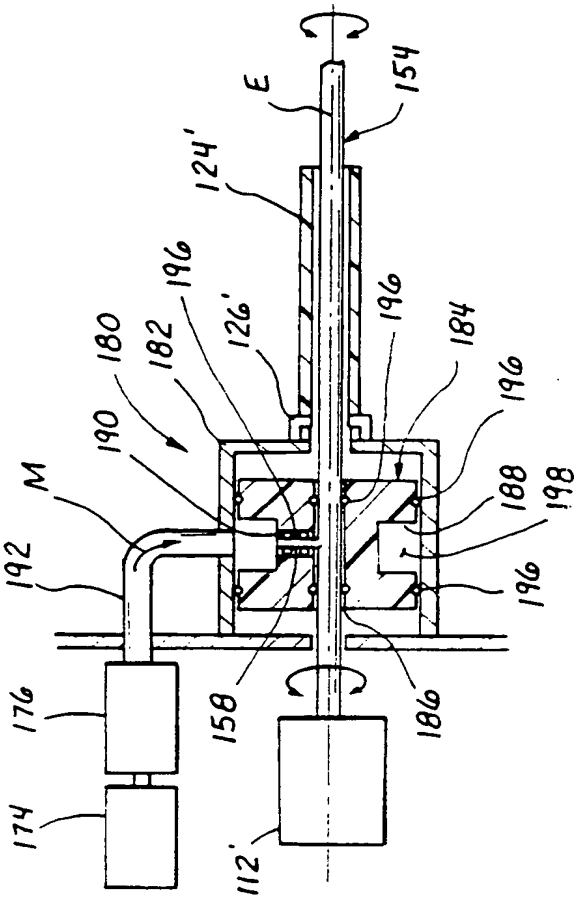


Fig. 19

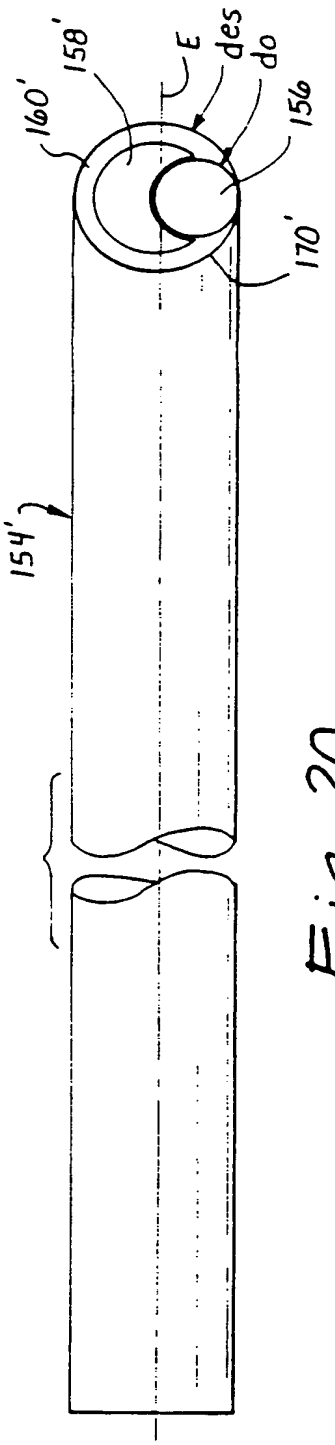


Fig. 20

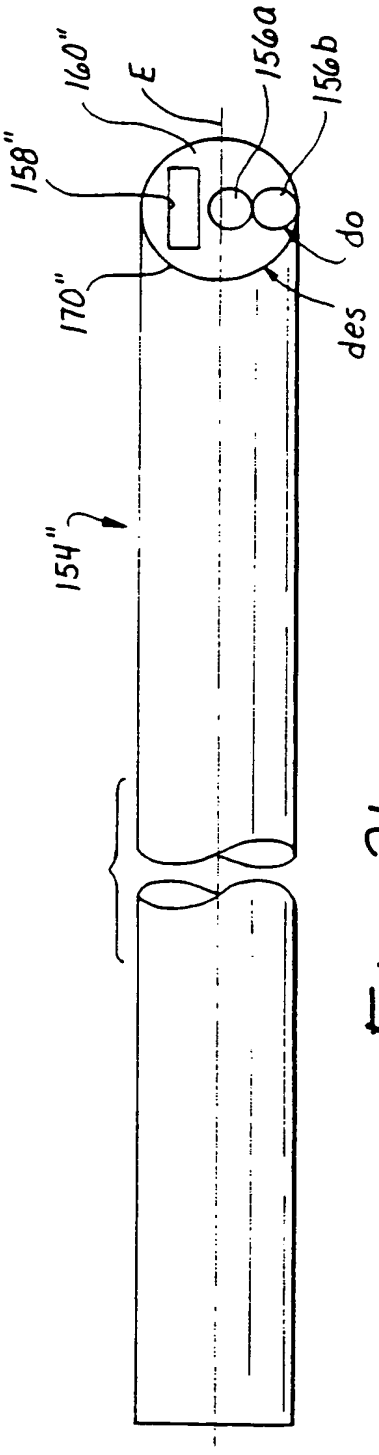


Fig. 21

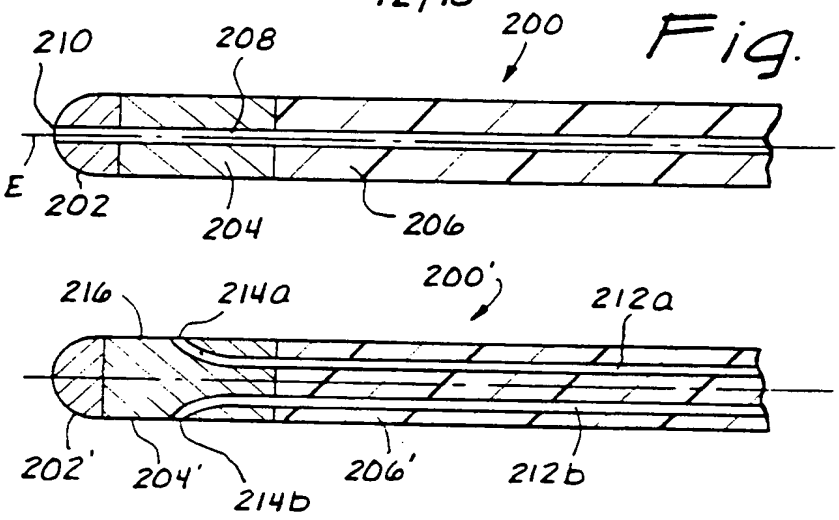
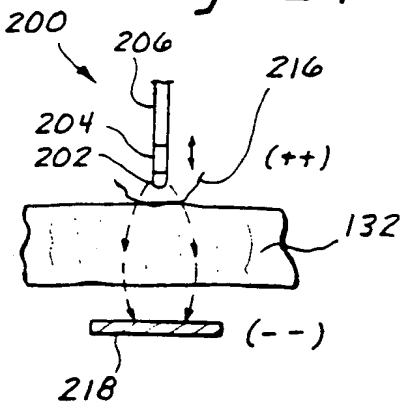


Fig. 22

Fig. 23

Fig. 24



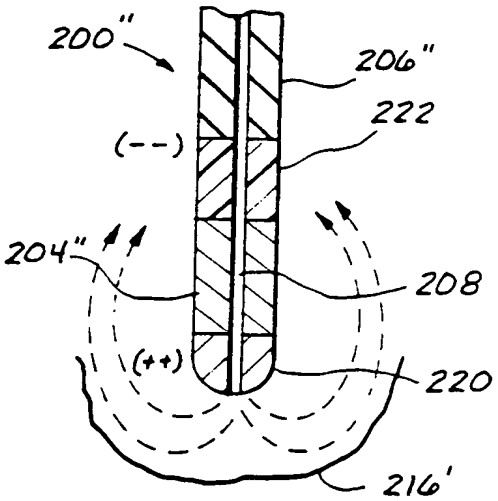


Fig. 26

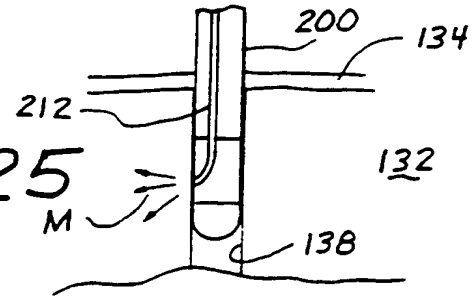


Fig. 25

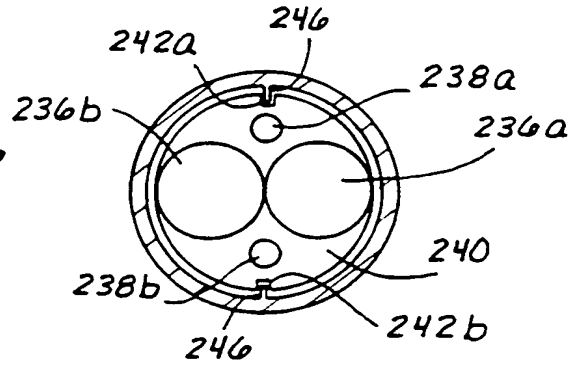


Fig. 27

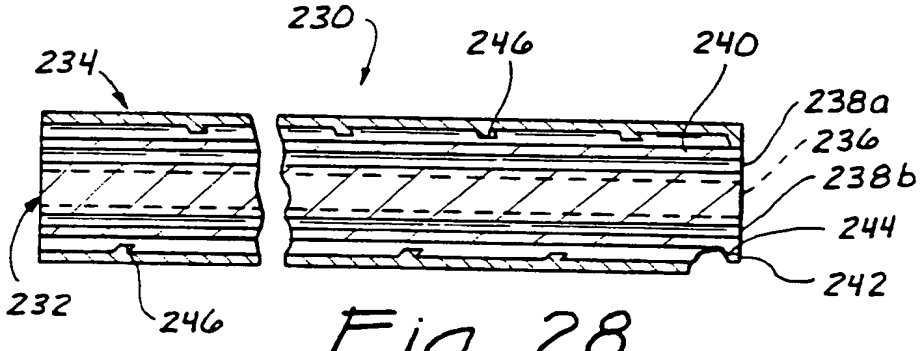
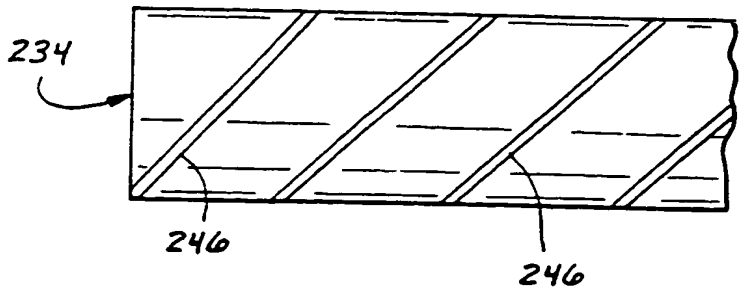


Fig. 28

Fig. 29



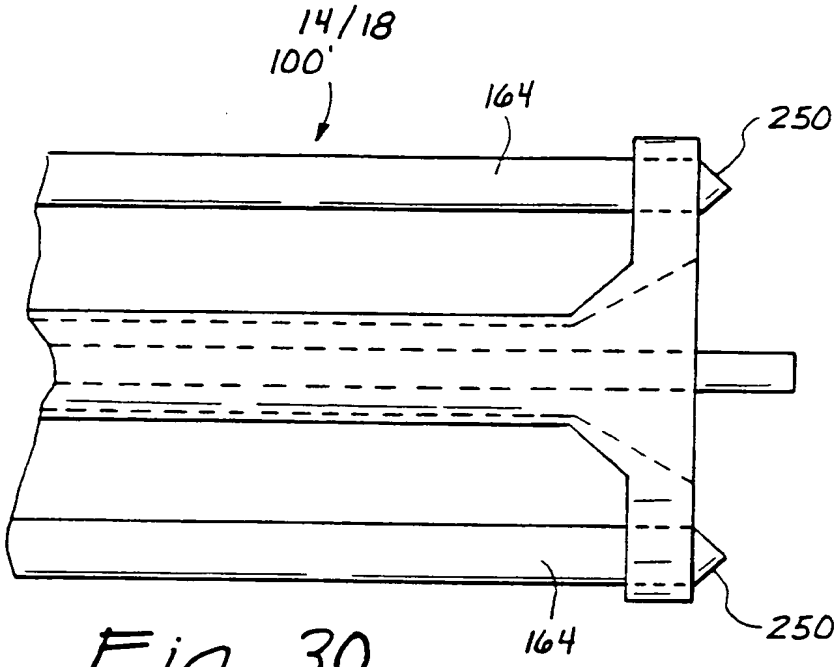


Fig. 30

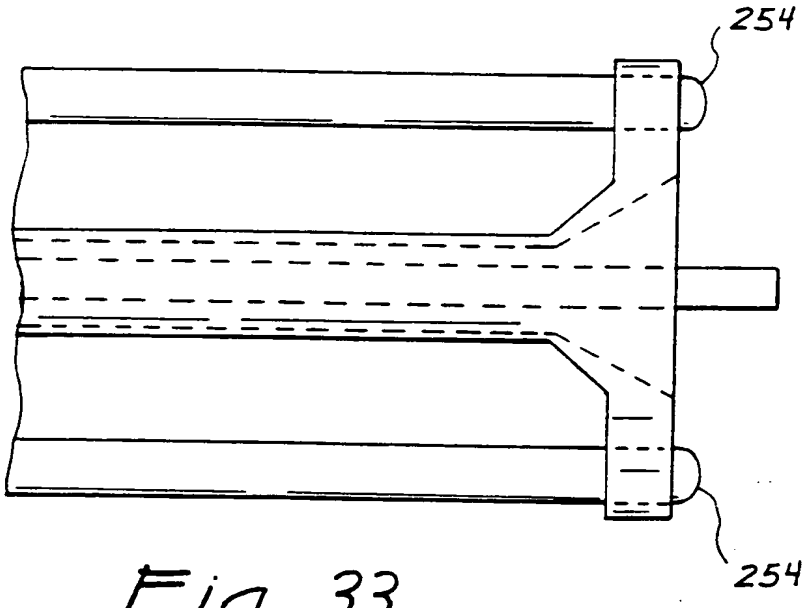


Fig. 33

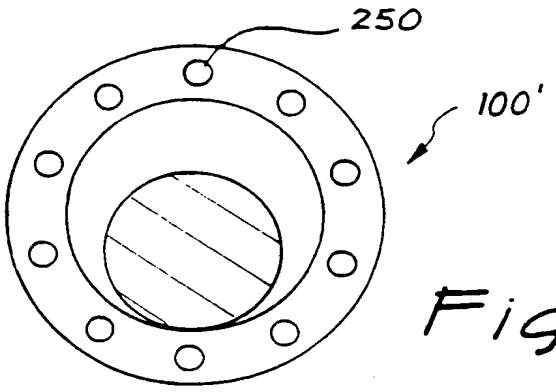


Fig 31

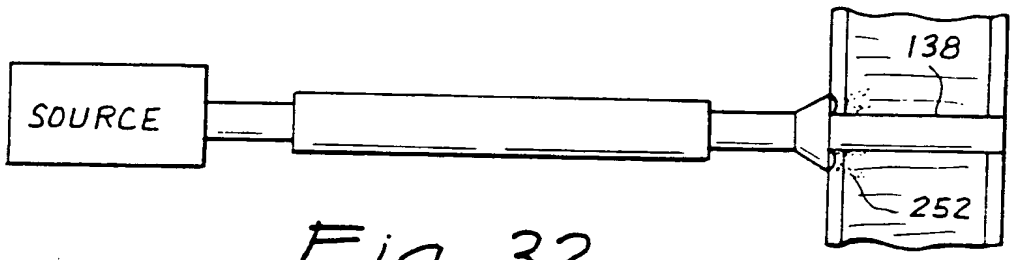


Fig. 32

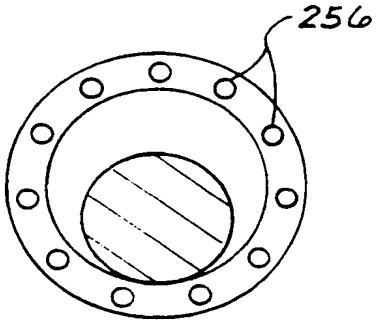


Fig. 34

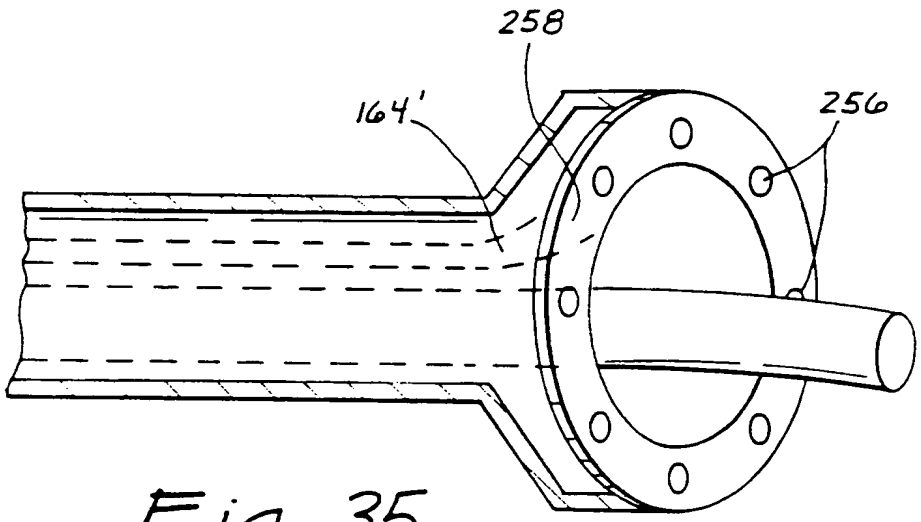


Fig. 35

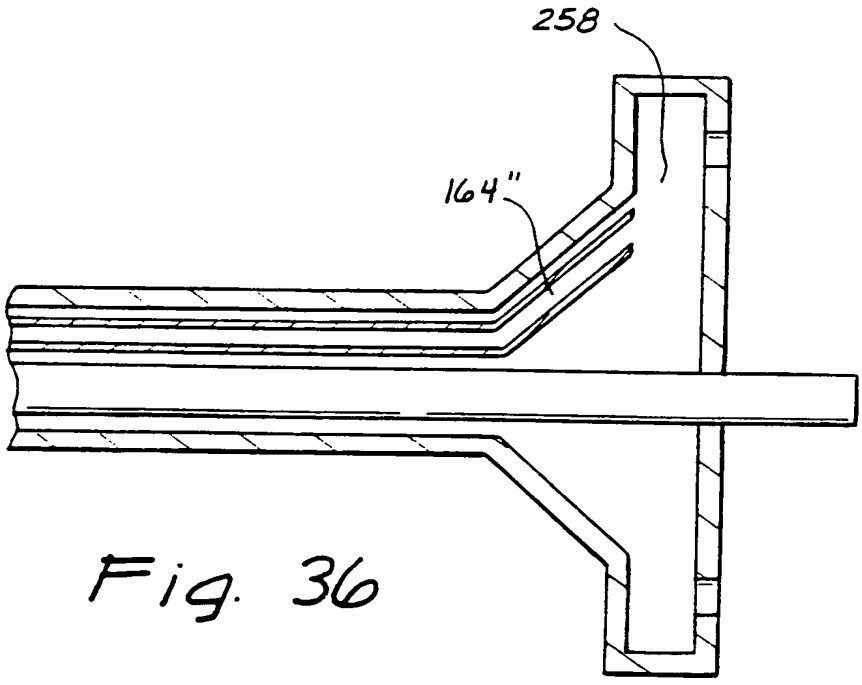
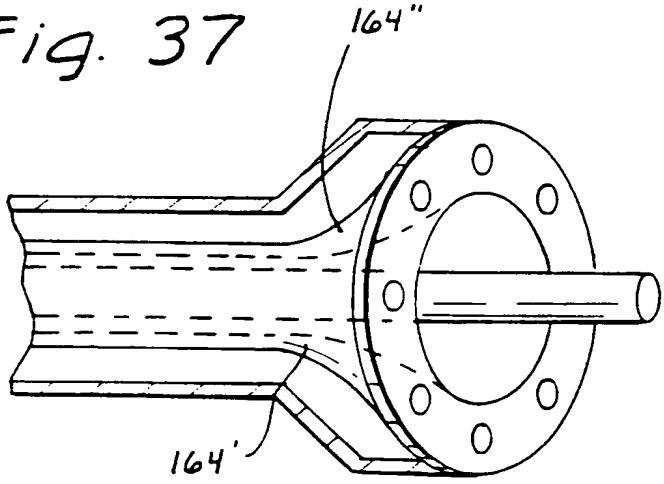


Fig. 36

Fig. 37



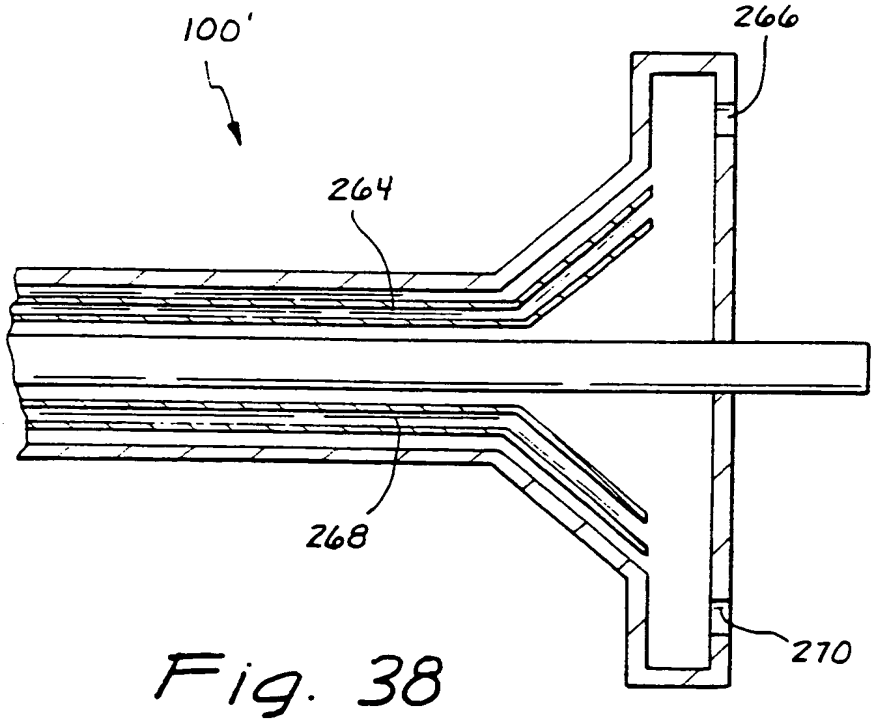


Fig. 38

Fig. 39

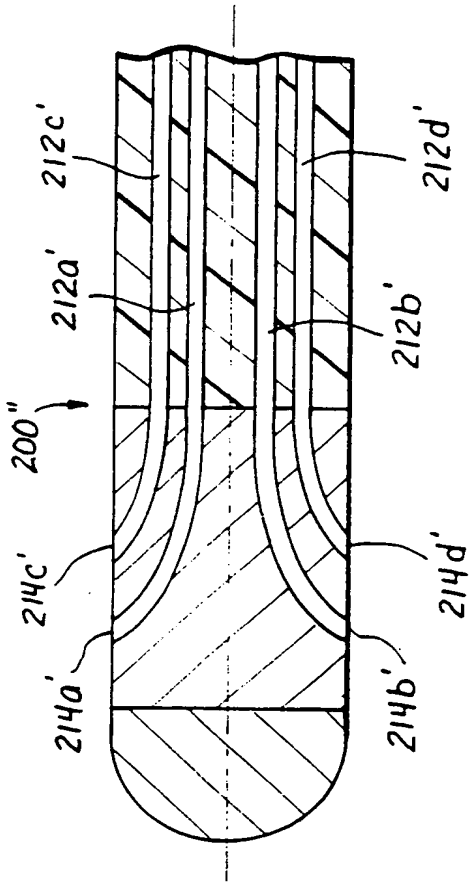
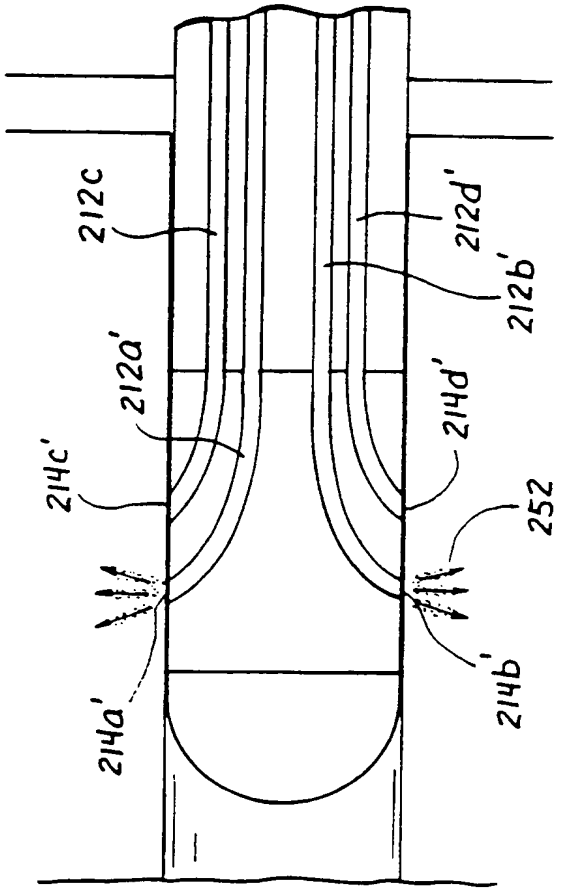


Fig. 40



INTERNATIONAL SEARCH REPORT

Inter onal Application No
PCT/US 99/28570

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B18/24

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 853 921 A (ECLIPSE SURGICAL TECH) 22 July 1998 (1998-07-22)	1-4,7,8, 22,23, 25-27, 29,41, 43,44
Y	page 21, line 37 - line 46; figure 12	46,50
A	page 24, line 7 - line 18; figure 16	5,6
X	WO 99 39624 A (BIOSENSE INC) 12 August 1999 (1999-08-12) page 20, line 15 - line 28; figure 6A	7,26,27, 29,41-44
X	WO 99 44516 A (BSC NORTHWEST TECHNOLOGY CENTE) 10 September 1999 (1999-09-10) page 5, line 17 - line 21; figure 2	22,26,41

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
31 July 2000	07/08/2000

Name and mailing address of the ISA	Authorized officer
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INTERNATIONAL SEARCH REPORT

Inte 'onal Application No
PCT/US 99/28570

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 19614 A (FOGARTY THOMAS J) 14 May 1998 (1998-05-14) page 26, paragraph 3 -page 27, paragraph 1; figure 23	22, 24-26, 28,29, 41,43,45
X	WO 96 35469 A (CARDIOGENESIS CORP) 14 November 1996 (1996-11-14) page 8, line 16 - line 27 page 18, line 24 - line 26; figure 14	51
Y	US 5 972 013 A (SCHMIDT CECIL C) 26 October 1999 (1999-10-26)	46,50
A	column 4, line 44 -column 5, line 20; figures 2,3	47

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-8,22-29,41-45

   energy source and medicament delivery system with handpiece

2. Claims: 46-50

   energy source and medicament delivery system with vacuum source

3. Claim : 51

   injection jet nozzle and medicament delivery system

INTERNATIONAL SEARCH REPORT

.formation on patent family members

Inter onal Application No
PCT/US 99/28570

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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		EP 1014871 A	05-07-2000
		WO 9913785 A	25-03-1999